Gastroenterology

Lectures

Diseases of the Esophagus

Anatomy:

- It is a muscular tube approximately (10 inch)25 cm long connecting the hypopharynx to the stomach.
- Lies posterior to the trachea
- Divided into three parts: cervical, thoracic and abdominal
- The muscle coat has 2 layers an outer longitudinal and inner circular layer.
- In the upper 1/3 both layers are striated muscle
- In the lower 2/3 both layers are smooth muscle.
- It is lined by stratified squamous epithelium except below the GI junction where it is lined with columnar epithelium.
- The esophagus is separated from the pharynx by UES which is usually closed by the continuous contraction of the cricopharyngeal muscle.
- The LES consists of an area of the distal end of esophagus which has a high-pressure resting zone app.20mmHg above gastric baseline and is largely responsible for the prevention of reflux.

Physiology of swallowing:

- During swallowing the bolus of food is moved from the mouth to the pharynx voluntarily. Immediately the UES relaxes and food enter the esophagus.
- A 1^{ry} peristaltic wave starts at the pharynx to push the food to the LES which relaxes to the gastric baseline allowing the food to pass to the stomach.
- 2^{ry} peristalsis occurs locally in response to distension and helps to clear food residue from the esophagus.
- Contraction of swallowing in the upper third is central while in lower two third is by local nerve plexus

Dysphagia

- Subjective awareness of difficulty in swallowing due to impaired progression of food from the pharynx to the stomach. (difficulty in swallowing), while odynophagia is painful swallowing
- **Causes: either functional(psychological) or organic**
  1. **Preoesophageal causes.**
  2. **Esophageal motility/structural disorders.**
  3. **Extrinsic pressure** (Mediastinal glands , Retrosternal goiter , Enlarged L" atrium)
  4. **Intrinsic lesions.**

  ➢ ***Organic causes of dysphagia***

  1. Preoesophageal(oropharyngeal) causes.

- Difficulty of emptying food material from the oropharynx into the esophagus (difficulty in initiating swallowing)
- It results from neuromuscular disorder as Myasthenia Gravis, Bulbar poliomyelitis, pseudobulbar syndrome.
- It is usually associated with nasal regurge, choking, aspiration pneumonitis.
- on examination, drooling, dysarthria, hoarseness, neurological deficit

2. Esophageal causes

➢ ***Motility disorder***

{Achalasia, Diffuse esophageal spasm}

➢ ***Structural***

{benign / malignant stricture, foreign body, rings, diverticula,}

- Foreign bodies (coins, pins, niddles,….)
- Stricture which may be
  a. **Benign**: GERD, corrosives, radiotherapy, injection sclerotherapy, post band, post APC, traumatic N.G intubation.
  b. **Malignant** (carcinoma)
- Lower Esophageal Ring [Schatzki Ring]

Narrowing of lower end of O due to a ridge of mucosa or fibrous membrane.

- **Upper O web (Plumer Vinson /petrsson Kelly)**

Atrophy of the squamous epithelium in the post cricoid region near the upper sphincter with formation of web

1. Dysphagia/ Odynophagia
2. Iron def. anemia
3. Atrophic glossitis
4. Angular stomatitis

it is one of the risk factors for developing squamous cell carcinoma of the oral cavity, esophagus, and hypopharynx.

- **Diverticula**

Pouch lined in epithelium which can produce dysphagia and regurgitation:

1. **Zenker's**: upper esophageal (above UOS),
2. **Traction**: mid Esophageal
3. **Epiphrenic**: lower esophageal (above LOS)

Motor disorders of the esophagus

Achalasia

Disease of unknown etiology characterized by aperistalsis of the body of the esophagus and failure of relaxation of LES on initiation of swallowing.

- **Pathology**

Degenerative lesions are found in the vagus nerve supply of Esophagus as well as decrease of ganglionic cells in the nerve plexus of the esophageal walls.

- **Clinical picture**

- Occurs at any age usually middle age between 20-40 years.
- Rare disease 1/100,000
- Gradual onset of dysphagia over months or year.
- Dysphagia for both solids and liquids.
- Other symptoms: regurgitation, chest pain, nocturnal cough.

- Predisposes to squamous cell carcinoma
- Regurgitation of undigested food occurs in 33% and may cause cough, pulmonary aspiration with lung abscess, pneumonia or bronchiectasis.
- Chest pain on swallowing.
- Weight loss is usually mild to moderate but severe weight loss should suspect achalasia 2ry to a tumor of GE junction.

➢ Diagnosis

1. Barium swallow: prestenotic dilatation of the esophagus with tapering smooth lower end (parrot pick deformity) due to failure of the sphincter to relax.
2. Upper endoscopy:
    - Essential to exclude carcinoma of the O
    - Dilated esophagus and the endoscope can pass the narrow sphincter to the stomach easily by its weight.
3. Esophageal manometry
    - A peristalsis of the body of the esophagus
    - Increased pressure of LES

➢ Treatment

1. Long term nitrates, calcium channel blocker to lower the resting LOS pressure.
2. Dilatation of LES by pneumatic balloon to weaken LOS.
3. Direct injection of Botulinum toxin into LOS (chemical denervation of cholinergic nerves in the distal esophagus).
4. Heller's operation: surgical division of the muscle coat of the lower esophagus sphincter.
5. POEM: Per Esophageal Endoscopic Myotomy

Symptomatic Diffuse Esophageal Spasm

A generalized neurogenic disorder of the esophageal motility in which phasic non propulsive contraction replace normal peristalsis; and in some cases LOS malfunction occur.

This type of spasm is an irregular, uncoordinated squeezing of the muscles of the esophagus.

➢ Clinical Picture

Severe retrosternal chest pain with dysphagia for both liquids and solids. The pain may awaken the patient from sleep. Very hot and cold liquids may aggravate the pain. The disorder may evolve into achalasia.

➢ Diagnosis

- Barium study: may show poor progression of Barium bolus or cork screw appearance.
- Manometric study: show repetitive, high amplitude, non peristaltic control or spasm and in 30% there is LES pressure and relaxation impairment.

➢ Treatment

- Anticholinergic, Nitroglycin, long acting nitrates.
- Calcium channel blocker (Verapamil 80 mg 3 hrs.).
- Pneumatic dilatation and Bougieonage may be helpful.
- Surgical myotomy along the full length of the O in intractable cases.

GERD

Factors which contribute to the competence of GE junction (HPZ):

1. Intrinsic sphincter pressure
2. The angle of cardio esophageal junction
3. The action of the diaphragm
4. Gravity
5. Increased intra abdominal pressure
6. Local neutralizing effect of saliva

GERD lead to esophagitis(damage to the esophageal mucosa due to the

- Caustic nature of the refluxate and the inability to clear the refluxate from the esophagus.
- Volume of gastric contents
- Decrease local mucosal protective mechanism.

The condition is predisposed by:

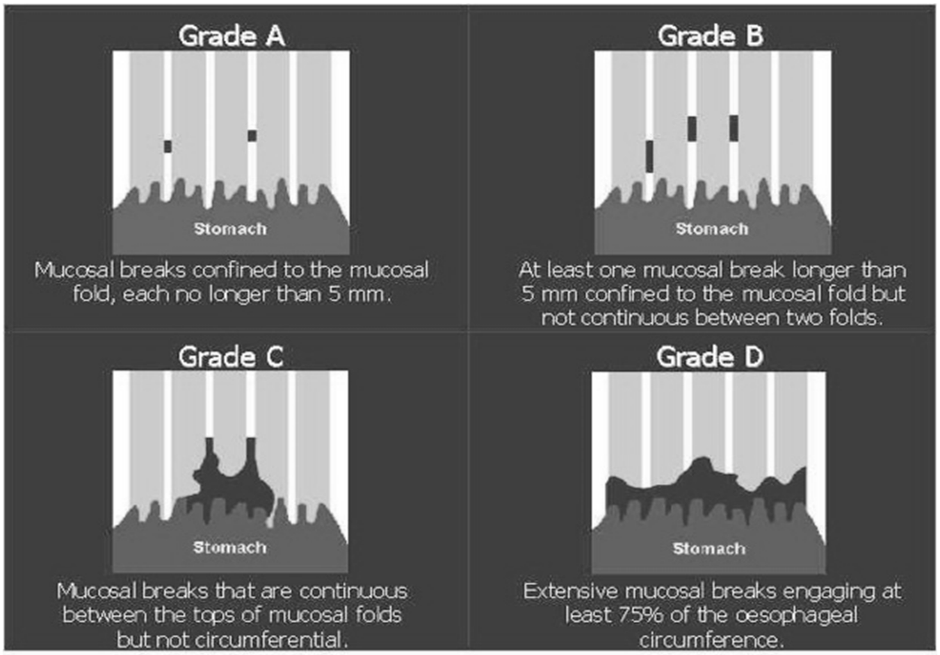
1. Obesity
2. Excessive intake of fatty diet, chocolate, coffee and cola drinks.
3. Smoking
4. Drugs: anticholinergic drugs, NSAID
5. Disease as systemic sclerosis, Achalasia and Hiatus hernia.

Clinical Picture

1. Heart Burn (Pyrosis): feeling of substernal burning pain that radiates upward from the epigastrium toward the neck occurring within one hour after meals and increased by maneuver that increase the intraabdominal pressure.
2. Odynophagia: (Substernal pain on swallowing) may occur in esophagitis (long standing reflux).
3. Stricture and dysphagia**.**

Diagnosis:

- Barium swallow: shows the reflux - stricture - ulcer - Achalasia - Hiatus hernia.
- Upper endoscopy: identify the degree of GERD(LA class.), to rule out stricture - ulcer - achalasia - Hiatus hernia and to take Biopsy from GE junction to rule out the presence of Barret's epithelium.
- Esophageal manometric study : which may show decreased tone of the LES.
- Bernstein Acid perfusion test : Simulation of GER by instillation of 0.1 N HCl into the lower esophagus.


Grade A
Stomach
Mucosal breaks confined to the mucosal fold, each no longer than 5 mm.
Grade B
Stomach
At least one mucosal break longer than 5 mm confined to the mucosal fold but not continuous between two folds.
Grade C
Stomach
Mucosal breaks that are continuous between the tops of mucosal folds but not circumferential.
Grade D
Stomach
Extensive mucosal breaks engaging at least 75% of the oesophageal circumference.

Complications

1. Peptic stricture which can lead to dysphagia.
2. Hematemesis from peptic ulceration of the lower esophagus.
3. Barrett's epithelium: Barrett's esophagus is a serious complication of GERD which is a premalignant condition. Simple columnar metaplasia in the cells of the lower portion of the esophagus. It is characterized by the replacement of the normal stratified squamous epithelium lining of the esophagus by simple columnar epithelium with goblet cells (which are usually found lower in the gastrointestinal tract). The medical significance of Barrett's esophagus is its strong association (about 0.5% per patient-year) with esophageal adenocarcinoma

➢ **Treatment**

Lifestyle Modification:

1. Decrease body weight.
2. Avoid fatty diet, acidic foods.
3. Avoid sleeping after meals.
4. Elevation of the head of the bed by 6 inches.
5. Stop smoking, drugs, chocolate, coffee, cola as they decrease L.E.S pressure.
6. **H_2 Blockers - Proton Pump inhibitors**

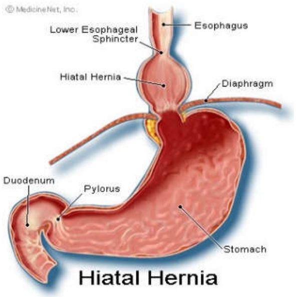
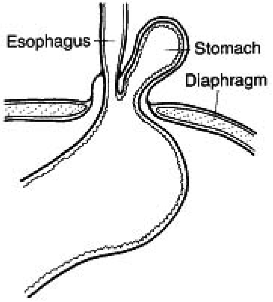
Cimetidine	**Omeprazole**
Ranitidine	**Pantoprazole**
Famotidine	**Lansoprazole**
Nizatidine	

7. **Prokinetic drugs to LES pressure**
    - **Cholinergic agonists (Bethanecol 25 mg 3 times)**
    - **Metoclopramide 10 mg 3 times**
    - **Domperidone**
    - **Itopride**

8. **Treatment of complications**
    - **Hemorrhage unless massive does not require emergency surgery.**
    - **O. stricture: Dilatation with Hg filled Bougies or with endoscopically placed balloons.**
    - **Resistant cases: surgery as fundoplication which can be performed laparoscopically**
    - **Barret's epithelium: intensive medical therapy or surgically, with follow up endoscopically.**
9. **Treatment of Helicobacter Pylori infection**

Hiatus Hernia

- **Protrusion of the stomach above the diaphragm.**
- **Types of HH : Sliding HH , Paraoesophageal HH**

Sliding HH	**Paraoesophageal HH**
 © MedicineNet, Inc. Lower Esophageal Sphincter Esophagus Hiatal Hernia Diaphragm Duodenum Pylorus Stomach Hiatal Hernia	
Gastroesophageal junction slides through the hiatus so that lies above the diaphragm	**Small part of the stomach rolls up through the hiatus alongside of the O. The GE junction still remain below the Diaphragm**
▪ **common - seen by X Ray in 40% of population** ▪ **most patients are asymptomatic** ▪ **but may produce chest pain** ▪ **GERD occurs in few patients** ▪ **Occult or massive GIT hemorrhage may occur with either type of HH**	▪ **asymptomatic but may incarcerate or strangulate.**

Diagnosis:

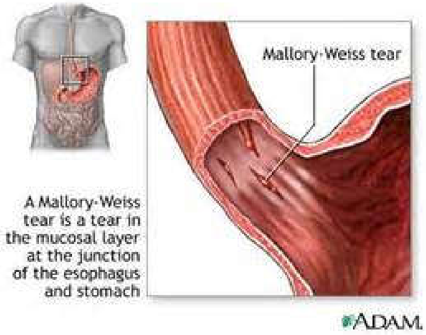
Barium study /endoscopy

Treatment:

- **Antacids - H_2 Blocker**
- **Surgery for paraoesophageal HH**

  For fear of risk of strangulation

Mallory Weiss Syndrome


Mallory-Weiss tear
A Mallory-Weiss tear is a tear in the mucosal layer at the junction of the esophagus and stomach
ADAM.

Linear mucosal tear occurring at the esophagogastric junction and produced by sudden increase of the intraabdominal pressure after bout of cough or vomiting producing hematemesis which usually stop spontaneously and rarely blood transfusion & injection of adrenaline endoscopically is required.

Boerhoave's syndrome (Esophageal perforation)

- **After forcible instrumentation (endoscope) causing severe epigastric pain and lower substernal pain radiating to the back with minimal hematemesis and surgical emphysema.**
- **Fatal condition- needs thoracotomy and closure of the perforation.**

Eosinophilic esophagitis (EOE)

EoE represents a chronic, immune/antigen mediated, oesophageal disease characterised clinically by symptoms related to oesophageal dysfunction and histologically by eosinophil-predominant inflammation

➢ **prevalence:**

* ***Atopic male (male/female ratio 2:1 to 3:1) presents in childhood or during the third or fourth decades of life***

* ***White, non-Hispanic***

* ***Prevalence is increasing with rate 6-30 cases/100,000***

* ***EoE in the United States 52/100,000***

➢ ***Diagnostic criteria Gastroenterology Consensus 2007***

1. ***Oesophageal symptoms***
2. ***>15 Eosinophils per HPF (X400)***
3. ***Lack of response to PPI***
4. ***Normal pH monitoring***

- ***Presentation of EOE***

* ***Dysphagia is the most common symptom***

(15% of patients with dysphagia have EOE on random biopsies)

* ***Food impaction is even more common***

* ***Refractory GERD is an important presentation (1-4%)***

- ***Endoscopic findings***

1. **Fixed esophageal rings (corrugated rings or trachealization)**
2. **Transient esophageal rings (feline folds or felinization),**
3. **Whitish exudates**
4. **Longitudinal furrows**
5. **Mucosal Edema**
6. **Diffuse esophageal narrowing**
7. **Narrow-caliber esophagus**
8. **Esophageal lacerations by passage of the endoscope**

Peptic Ulcer Diseases

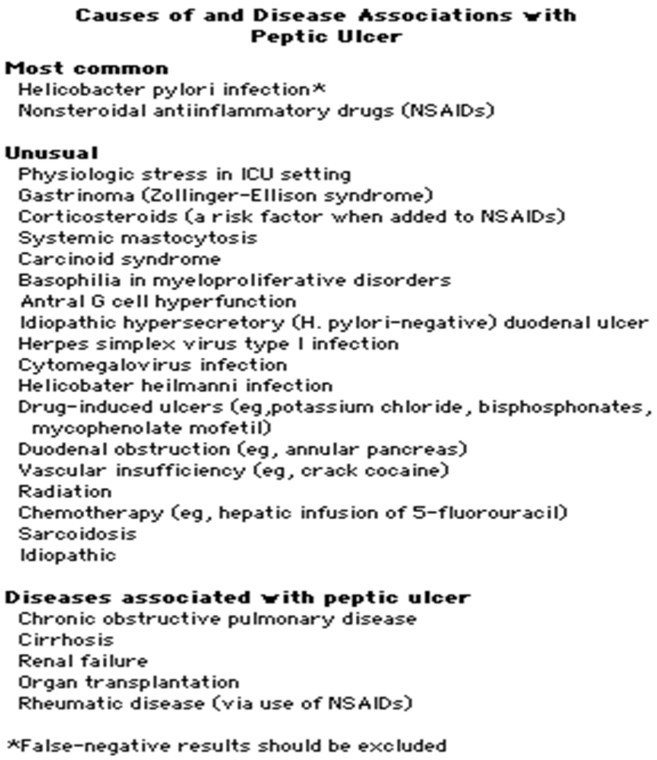
- **Responsible for 10 % of medical costs for digestive diseases**
- **Natural history**
  - **Resolution**
  - **Complications**
    - **Bleeding**
    - **Perforation**
    - **Obstruction**
- **Natural History :**

✓ **Pt's ulcer history predicts future behavior**

✓ **Those with history of complications have an increased risk of future complications.**

✓ **Ulcers refractory to initial healing are likely to rapidly recur & ulcers that have recurred are likely to continue to do so.**

✓ **Long duration of symptoms prior to presentation is more likely to be assoc. w' poor response to therapy.**



Causes of and Disease Associations with Peptic Ulcer

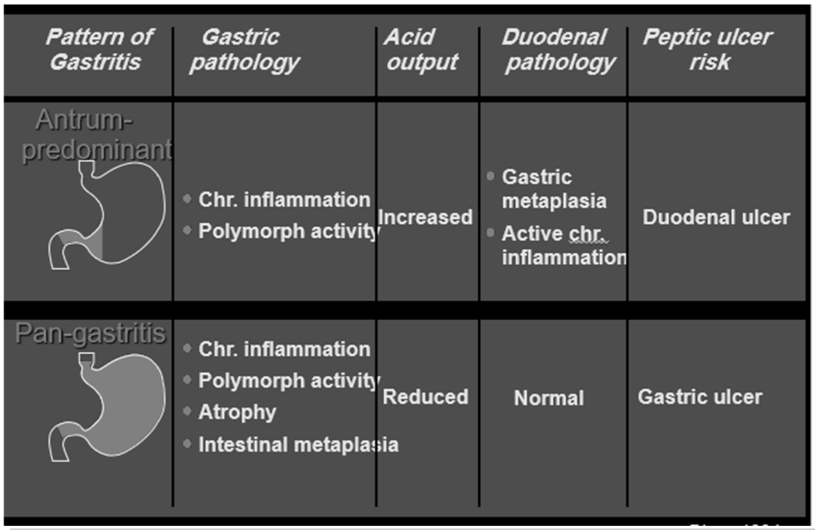
Most common
- Helicobacter pylori infection*
- Nonsteroidal antiinflammatory drugs (NSAIDs)

Unusual
- Physiologic stress in ICU setting
- Gastrinoma (Zollinger-Ellison syndrome)
- Corticosteroids (a risk factor when added to NSAIDs)
- Systemic mastocytosis
- Carcinoid syndrome
- Basophilia in myeloproliferative disorders
- Antral G cell hyperfunction
- Idiopathic hypersecretory (H. pylori-negative) duodenal ulcer
- Herpes simplex virus type I infection
- Cytomegalovirus infection
- Helicobater heilmanni infection
- Drug-induced ulcers (eg,potassium chloride, bisphosphonates, mycophenolate mofetil)
- Duodenal obstruction (eg, annular pancreas)
- Vascular insufficiency (eg, crack cocaine)
- Radiation
- Chemotherapy (eg, hepatic infusion of 5-fluorouracil)
- Sarcoidosis
- Idiopathic

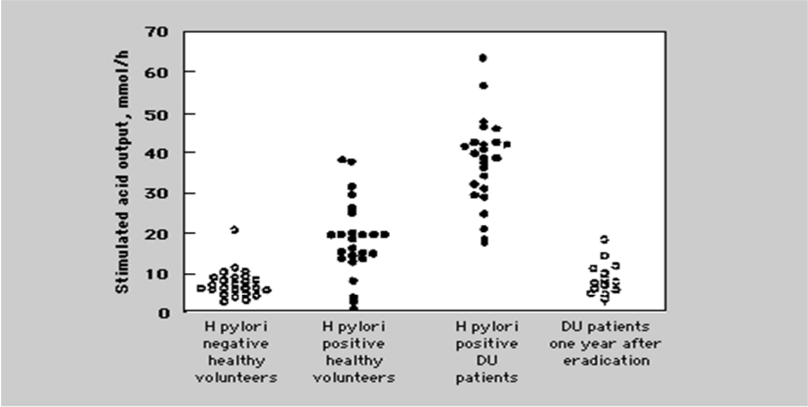
Diseases associated with peptic ulcer
- Chronic obstructive pulmonary disease
- Cirrhosis
- Renal failure
- Organ transplantation
- Rheumatic disease (via use of NSAIDs)

*False-negative results should be excluded

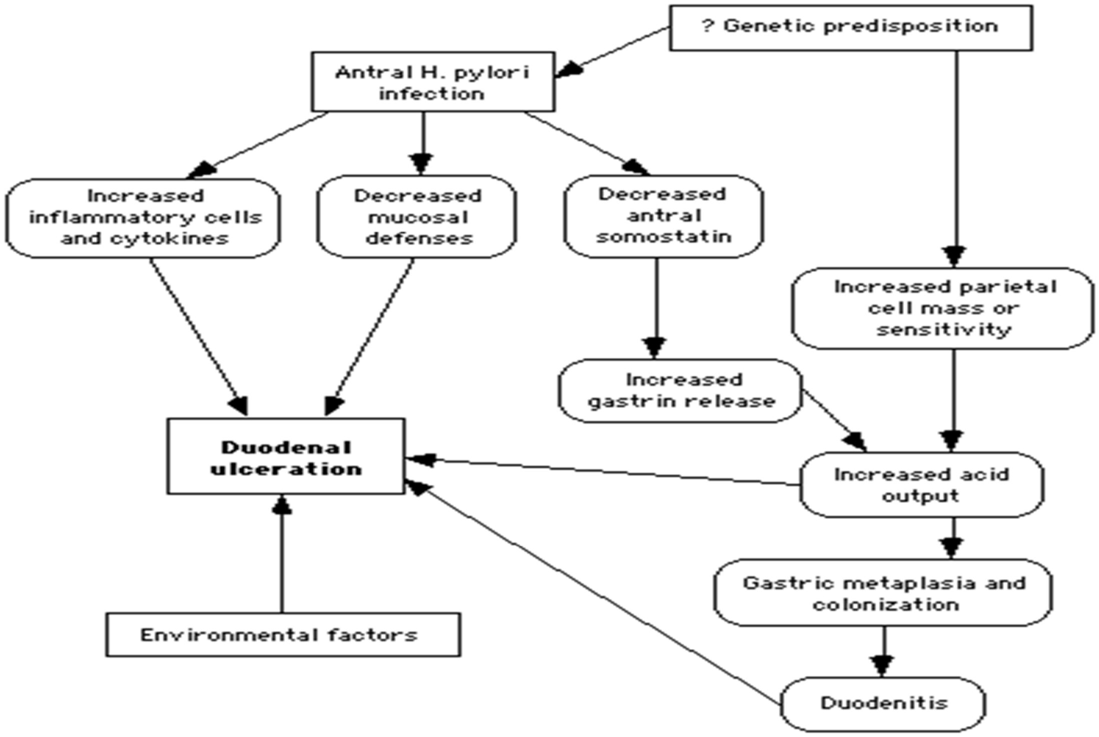
- **H.Pylori Disease Implications**
- **Gastritis**
- **PUD**
- **Gastric CA**
- **MALT Lymphoma**
- **Functional Dyspepsia**
- **GERD**
- **NSAID**
- **Two patterns of H. pylori Gastritis**



Pattern of Gastritis	*Gastric pathology*	*Acid output*	*Duodenal pathology*	*Peptic ulcer risk*
Antrum-predominant	Chr. inflammation Polymorph activity	Increased	Gastric metaplasia Active chr. inflammation	Duodenal ulcer
Pan-gastritis	Chr. inflammation Polymorph activity Atrophy Intestinal metaplasia	Reduced	Normal	Gastric ulcer



Gastric acid secretion and Helicobacter pylori infection
Gastric acid secretion in response to stimulation with gastrin-releasing peptide in subjects of different Helicobacter pylori status. Stimulated acid output is increased in infected volunteers and, to a greater degree, in infected patients with duodenal ulcer (DU). This response returned to normal one year after eradication of H. pylori. (Data from McColl, KEL. Helicobacter pylori: Clinical aspects. J Infect 1997; 34:7).


? Genetic predisposition
Antral H. pylori infection
Increased inflammatory cells and cytokines
Decreased mucosal defenses
Decreased antral somostatin
Increased parietal cell mass or sensitivity
Increased gastrin release
Duodenal ulceration
Increased acid output
Gastric metaplasia and colonization
Environmental factors
Duodenitis

Possible Mechanisms of Ulcerogenesis in Helicobacter pylori Infection

Reproduced with permission from the American College of Gastroenterology, (American Journal of Gastroenterology, 1997; 92:11S).

- **Extra digestive Manifestations of H. pylori**
  - **Vascular**
    1. **IHD**
    2. **Raynaud's phenom.**
    3. **Headache & migraine**
  - **Autoimmune**
    1. **Henoch-Schoenlein purpura**
    2. **Sjogren's syndrome**
    3. **ITP**
  - **Other**

Rosacea & urticaria   Sideropaenic anaemia

Growth retardation   Amenorrhoea & late menarche

Halitosis   Extra gastric MALT Lymphoma

NIDDM

- **Diagnosis of H. pylori:**
  - ***Endoscopy-based Invasive tests***
    1. **Rapid urease test**
    2. **Direct microscopy**
    3. **Histology**
    4. **Culture**
    5. **DNA probes/PCR**
  - ***Non-invasive Tests***
    1. **$^{13/14}$C-urea breath test (UBT)**
       Serology (lgG, lgA)
    2. **PCR in saliva and faeces**
    3. **Stool Hp antigen**

- **What Diagnostic test should I depend On**
  - **Screening for "latent" Infection:**
  - **Serology: Quick, Inexpensive, Reliable**
  - **Could be a "Scar" from past infection**
  - **Not actually reflect "Current" status**
  - **Positive Serology should be confirmed by :**
  - **UBT or Stool Ag**
  - **Treat Only on *Positive Confirmed* Results**
  - **During Endoscopy**

Take 2 Mucosal samples:

First: RUT if Positive start R

Second: Histopathology

Examine only when Neg. RUT

Treat Only on *Positive* Results

• Consensus on treating H.P *(i.e. Strongly Recommended):*

- **PUD**
- **Gastric Lymphoma**
- **Atrophic Gastritis**
- **Pts of Gastric CA post-Resection**
- **Close relatives of Gastric CA pts**

▸ Treatment Options

- **Antibiotics**
    1. **Clarithromycin**
    2. **Amoxycillin**
    3. **Metronidazole**
    4. **Tetracycline**
    5. **Furazolidone**
- **Adjuvant Drugs**
    1. **PPI**
    2. **RBC**

▶ Protocols of H.P Eradication

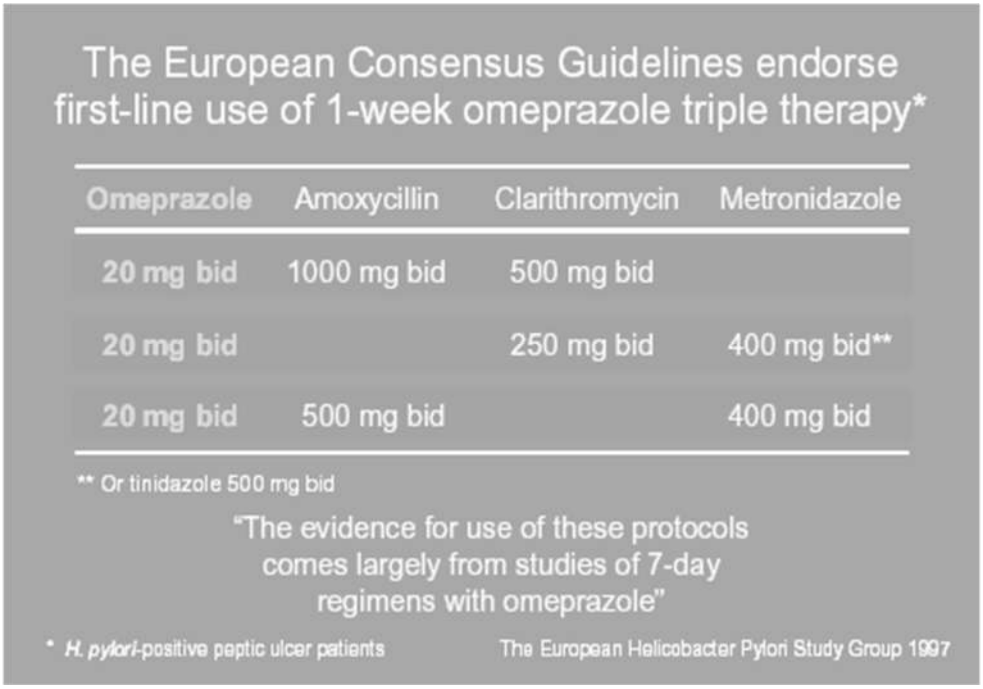
1. **Monotherapy**
2. **Dual Therapy = 1 A.B + 1 Adjuvant**
3. **Triple Therapy = 2 A.B + 1 Adjuvant**
4. **Quadruple Therapy = 2 A.B + 2 Adjuvant**

- **First Line Therapy**
    - **PPI-based Triple Therapies**
    - **Ranitidine Bismuth Citrate - Based Triple therapies**
- **Second Line Therapy**
- **Future Therapies**
- **PPI Based Therapies:**

• **Omeprazole**	**20 mg *twice* daily**
• **Lanzoprazole**	**30 mg**
• **Pantoprazole**	**40 mg**
• **Rabeprazole**	**20 mg**

- **Esomeprazole   40 mg**

PPI Based Triple Therapy
PPI   Bid
+
Clarithromycin 500 mg Bid
+
Amoxicillin 1000 mg Bid
or
Metronidazole 500 mg Bid



The European Consensus Guidelines endorse first-line use of 1-week omeprazole triple therapy*

Omeprazole	Amoxycillin	Clarithromycin	Metronidazole
20 mg bid	1000 mg bid	500 mg bid	
20 mg bid		250 mg bid	400 mg bid**
20 mg bid	500 mg bid		400 mg bid

** Or tinidazole 500 mg bid

"The evidence for use of these protocols comes largely from studies of 7-day regimens with omeprazole"

* *H. pylori*-positive peptic ulcer patients

The European Helicobacter Pylori Study Group 1997

Duration of Eradication Therapy

Regimens of very short Duration (< 7 d):

European Guidelines at least 7 days

Few reports of success of as short as 3-4 days treatment but usually with 3 A.B

Regimens with duration > 7 days:

American Guidelines: At least 10-14 days

10-14 days better in high "Bacterial load"

10 =14 days, but better than 7 days

Follow Up after Therapy

- **Recurrence of symptoms**
- **Endoscopy is required**
    - ***RUT***
    - ***Histo-Biopsy***
- **Endoscopy is *not* required**
    - ***UBT***
    - ***Stool Antigen***

Why not Serology

- **23 H.Pylori volunteers confirmed by biopsy**
- **Eradication confirmed by biopsy**
- **Serology was obtained monthly for 18 ms**
- **At 3 ms 50 % decrease in Ab titre**
- **At 18 ms 60 % of pts undetectable Abs**

  A serology after treatment should be done
  at least *ONE YEAR* after eradication

- **Check Only After > 4 Weeks**

- **Cure = No organism > 4 weeks after cessation of anti-microbial treatment**

- **A.B susceptibility available:**

  follow it

- **A.B susceptibility not available :**

Metro → Clarithromycin

Options After Failure of Eradication
Second Line Therapy

1. Quadruple therapy: 67-88 %

PPI Bid

+

Bismuth 2 Tab qid

+

Metronidazole 250 tid

+

Tetracycline 500 mg qid

For 10-14 Days

- ✓ **Adverse effects on mucosal aggressive & protective factors**
- ✓ **Studies in pre-H. pylori era found that smoking had facilitative role for PUD**
- ✓ **Smokers**
  - **More likely to develop ulcers**
  - **Ulcers were more difficult to treat**
  - **Higher rate of recurrence**
- ✓ **Does not appear to be a risk factor for ulcer relapse once H. pylori was eradicated from infected patients**
- ✓ **Ulcer relapse occurred in 3.6 % vs 2 % in nonsmokers, (not significant)**
- ✓ **Smoking did not effect H. p. recurrence**

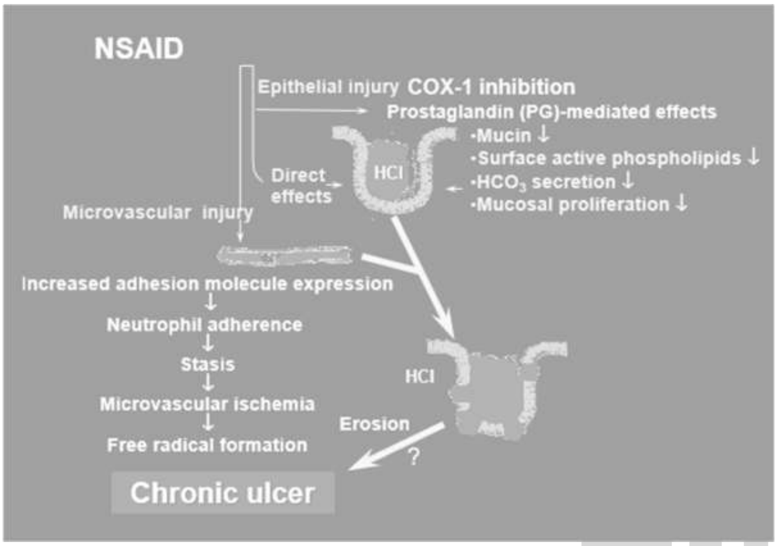
2. Rifabutin based therapy

PPI + Amox + rifabutin 72 % success

3. Consecutive Therapies 100 %

NSAIDs Associated risks?

- **Majority of PU not caused by H. pylori**
- **Assoc. w increased risk of complications**
- **Odds ratio for GU = 5.9 & DU = 4.9**
- **Odds ratio for hemorrhage was 5.2, as was perforation.**



- **NSAIDs are responsible for a significant number of PU refractory to therapy**
- **40 % of pts may not report using NSAIDs**
- **Pts w PU who must continue NSAIDs should be maintained on either PPI or H2RA**
- **COX-2 selective NSAIDs offer alternative.**

Gastrointestinal Lesions induced by NSAIDs

1. Acute Mucosal Lesions:

- **Petequia**
- **Erosions**
- **Acute Ulcers**

2. Chronic/Deep GD Ulcers

3. Complications:

- **GI Bleeding**
- **Perforation**
- **Obstruction**

Ulcer Size

- **Large and small GUs heal at the same rate on antacids, ~3 mm/wk.**
- **Ulcer healing was less likely in ulcers $\geq$ 10 mm in diameter (62 %), vs smaller ulcers (76%).**

Age and Sex

- **Onset of ulcer disease in youth & positive family history may be associated w poor healing**
- **Ulcers in older pts may heal more slowly**
- **Older pts are more likely to bleed, rebleed, require more transfusions, & have a prolonged hospital stay.**

Alcohol

- **Modest alcohol consumption does not appear to retard cure of PU**
- **Alcohol abuse interferes w ulcer healing**

Diet

- **Frequent feedings, cause less gastric distension, w may lead to sustained stimulation of acid secretion.**
- **Milk was a main therapy for PU because of its soothing nature, until it was shown to be a strong acid secretagogue, because of its calcium & protein content**
- **Milk stimulates more acid secretion than it buffers**
- **Milk use should not be discouraged in pts who find these measures beneficial**
- **Pts should be told that milk is not therapy for ulcer**

Clinical Picture of PU

Uncomplicated	Complicated
Nausea Anorexia Dyspepsia Abdominal Pain Vomiting Loss of Weight	○ Bleeding ○ Hematemesis – Coffee ground ○ Melena ○ Occult positive Anemia ○ Hematochezia (rare) ○ Obstruction ○ Vomiting of large amounts & post-prandially > 12 h ○ Succession Splash ○ Perforation ○ Severe abdominal pain ○ Hypotension / Shock ○ Rigidity ○ Rebound tenderness ○ Air under diaphragm

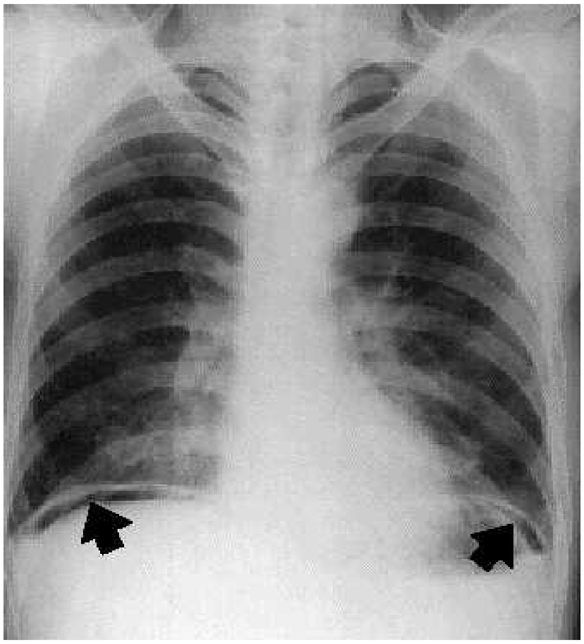
Diagnosis:

1. Barium Meal

- Diagnose Ulcer : Ulcer niche
- Diagnose Complications
    - Obstruction
    - Perforation
- Contraindicated during bleeding
- Can not diagnose healing of ulcer

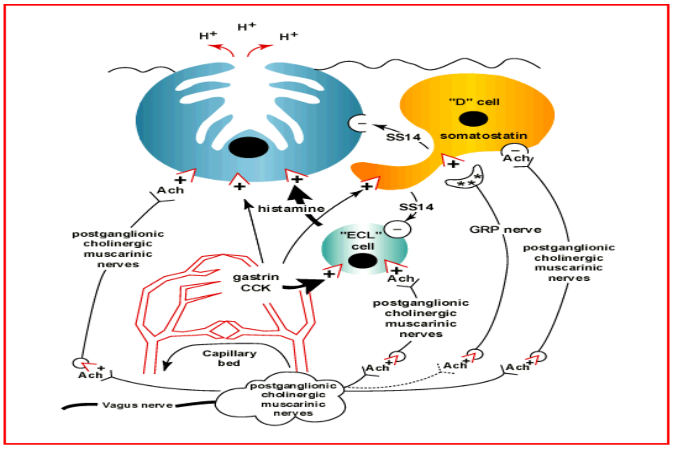
2. Plain X-ray

Air under diaphragm = Perforation



3. Endoscopy

- Diagnose Ulcer
- Biopsies for H.P &/or Malignancy
- Diagnose Complications
    - Bleeding
    - Obstruction
- Contraindicated in perforation
- Treatment of Bleeding ulcer
- Treatment of Obstructing Ulcer


H+
H+
H+
"D" cell
somatostatin
SS14
Ach
+
Ach
histamine
SS14
"ECL" cell
GRP nerve
postganglionic cholinergic muscarinic nerves
gastrin
CCK
Ach
postganglionic cholinergic muscarinic nerves
postganglionic cholinergic muscarinic nerves
Capillary bed
Ach
Ach
Ach
Ach
Vagus nerve
postganglionic cholinergic muscarinic nerves

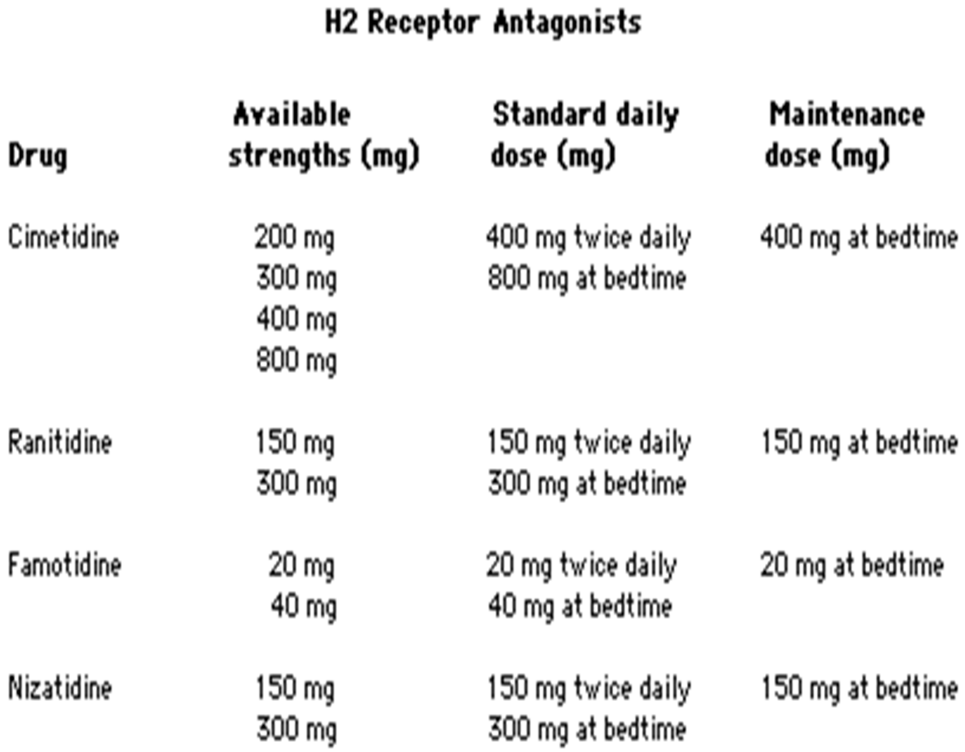
Regulation of acid secretion Release of histamine by gastrin from enterochrommafin-like cells (ECL, in green) appears to be the major physiologic mechanism by which gastrin stimulates acid secretion, although parietal cells (in blue) also have gastrin receptors. In addition, the ECL cells integrate stimulatory messages from cholinergic nerves and inhibition by locally released somatostatin. (Modified from Soll, AH, Berglindh, T. Receptors regulating acid secretory function. In: Physiology of the Gastrointestinal Tract, volume 1, Johnson, LR, Christensen, MJ, Jackson, ED, et al (Eds), Raven Press, New York,1994. p.11.)

Treatment:

1. **H.pylori Positive uncomplicated Ulcer**
2. **H.pylori unrelated uncomplicated ulcer**

➢ Drugs used in Treatment of PU:

1. **H2 RA**
2. **PPI**
3. **Prostaglandin**
4. **Anti - H.pylori therapy**



H2 Receptor Antagonists

Drug	Available strengths (mg)	Standard daily dose (mg)	Maintenance dose (mg)
Cimetidine	200 mg 300 mg 400 mg 800 mg	400 mg twice daily 800 mg at bedtime	400 mg at bedtime
Ranitidine	150 mg 300 mg	150 mg twice daily 300 mg at bedtime	150 mg at bedtime
Famotidine	20 mg 40 mg	20 mg twice daily 40 mg at bedtime	20 mg at bedtime
Nizatidine	150 mg 300 mg	150 mg twice daily 300 mg at bedtime	150 mg at bedtime

Pharmacokinetic Properties of PPI

Agent	Bio-Availability	$C_{max}^{\#}$	AUC_{0-24}^{D}	Excretion	pKa
Omeprazole	45%	07	2.0	Renal	4.0
Lansoprazole	85%	0.5-1.0	2.5	Biliary	4.0
Rabeprazole	52%	0.4	0.8	Renal	5.0
Pantoprazole	77%	1.5	5.0	Renal	3.9
Esomeprazole	64%		4.3	Renal	4.0

ACG Recommendations of PPI in Treatment of Acid-related Disorders

Active and maintenance therapy of gastro-duodenal ulcers:

Omeprazole – 20 mg

Lansoprazole – 30 mg

Rabeprazole – 20 mg

Pantoprazole – 40 mg

Esomeprazole - 40 mg

Prevention of NSAID-induced ulcers:

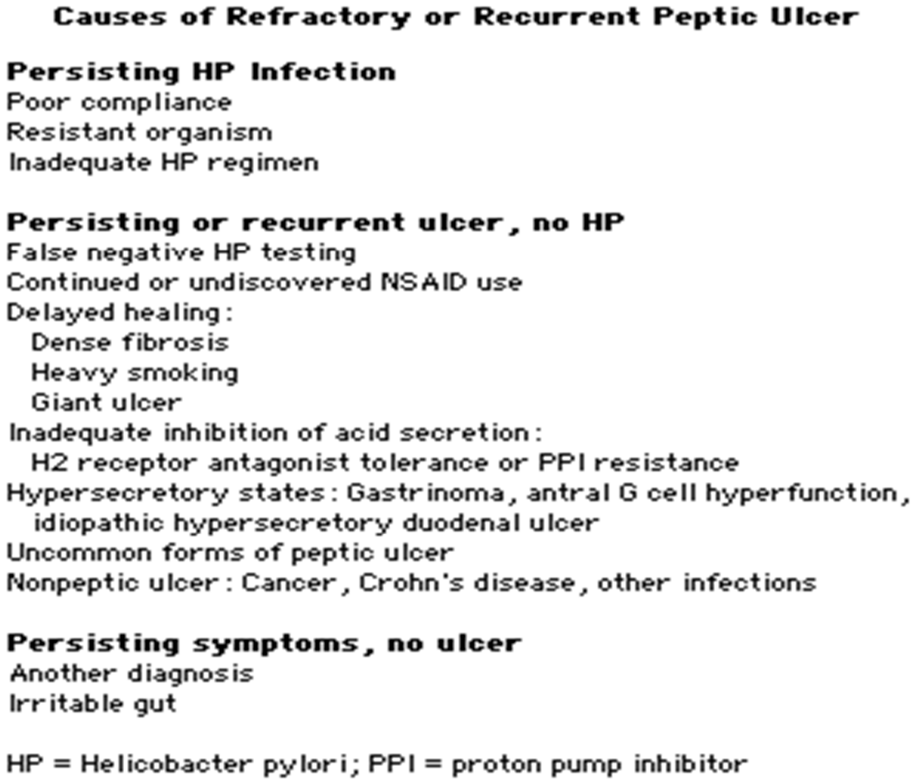
All PPIs above.

Comparison of Drug interactions with PPI

Concomitant drug	Omeprazole	Lansoprazole	Rabeprazole	Pantoprazole	Esomeprazole
Warfarin	PT decreased by 10%	-	-	-	-
Diazepam	$t_{1/2}$ increased by 130%	-	-	-	Decrease Clearance
Phenytoin	$t_{1/2}$ increased by 27%	-	-	-	-
Theophylline		AUC increased by 10%	-	-	Unknown
Digoxin	AUC increased by 10%	-	AUC, C_{max}, $t_{1/2}$ increased	-	Unknown
Carbamazepine	AUC increased by 75%	-	-	-	Unknown

Principal Cytochrome P450 Enzymes

PPI	Primary pathway	Secondary pathway	Sulfotransferase
• Omeprazole	CYP2C19	CYP3A4	No
• Lansoprazole	CYP3A4	CYP2C19	No
• Rabeprazole	CYP2C19	CYP3A4	No
• Pantoprazole	CYP2C19	CYP3A4	Yes
• Esomeprazole	CYP2C19	CYP3A4	No



Causes of Refractory or Recurrent Peptic Ulcer

Persisting HP Infection
Poor compliance
Resistant organism
Inadequate HP regimen

Persisting or recurrent ulcer, no HP
False negative HP testing
Continued or undiscovered NSAID use
Delayed healing:
  Dense fibrosis
  Heavy smoking
  Giant ulcer
Inadequate inhibition of acid secretion:
  H2 receptor antagonist tolerance or PPI resistance
Hypersecretory states: Gastrinoma, antral G cell hyperfunction, idiopathic hypersecretory duodenal ulcer
Uncommon forms of peptic ulcer
Nonpeptic ulcer: Cancer, Crohn's disease, other infections

Persisting symptoms, no ulcer
Another diagnosis
Irritable gut

HP = Helicobacter pylori; PPI = proton pump inhibitor

Treatment of Bleeding Ulcer:

1. **Hemodynamic Resuscitation**
2. **Anti-Helicobacter Therapy**
3. **Endoscopic Methods**
    - **Heater Probe**
    - **Coagulation**

- Sclerotherapy
- Band Ligation
- APC
- Laser Therapy

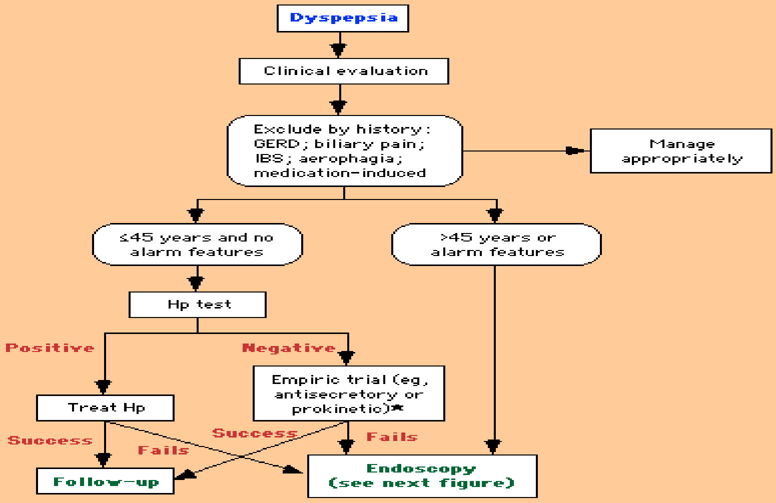
Treatment of Obstruction:

- Resuscitation
- NG suction of Gastric Contents
- Endoscopic Balloon Dilatation
- Surgical By-pass

Treatment of Perforation:

- Resuscitation
- NPO
- IV fluids
- IV A.B
- Immediate Surgical Closure (most)
- Endoscopic Clips
  - when noticed during endoscopy
  - Small
  - Recent

Evaluation of Dyspepsia-I†

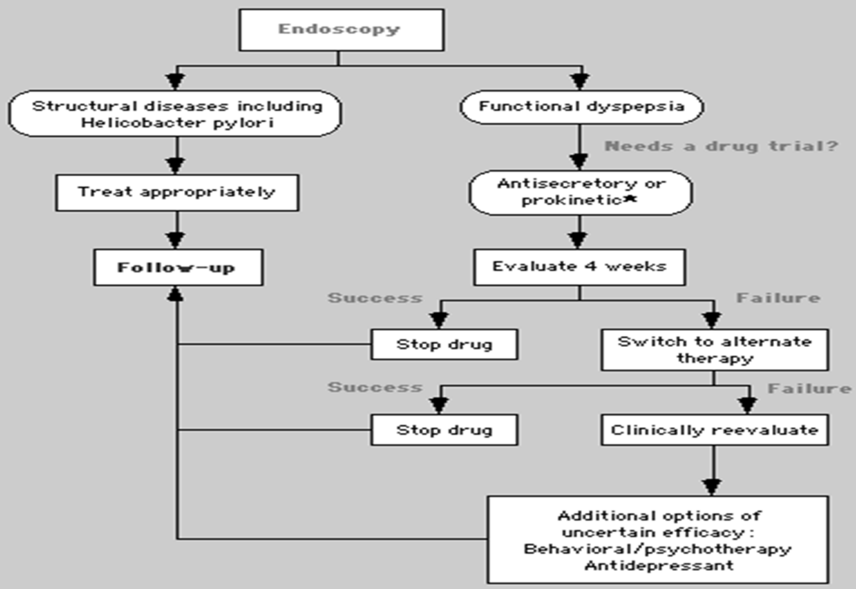

Dyspepsia
Clinical evaluation
Exclude by history: GERD; biliary pain; IBS; aerophagia; medication-induced
Manage appropriately
≤45 years and no alarm features
>45 years or alarm features
Hp test
Positive
Negative
Treat Hp
Empiric trial (eg, antisecretory or prokinetic)*
Success
Fails
Success
Fails
Follow-up
Endoscopy (see next figure)

GERD = gastroesophageal reflux disease; IBS = irritable bowel syndrome; Hp = Helicobacter pylori. The word 'fails' refers to symptomatic failure. Alarm features include unexplained weight loss, recurrent vomiting, dysphagia, evidence of anemia or gastrointestinal bleeding, or an abdominal mass or lymphadenopathy.

* Use of the prokinetic cisapride has been severely restricted in the United States because of concerns related to cardiac arrhythmias

† Adapted from American Gastroenterological Association. Medical Position Statement: Evaluation of dyspepsia. Gastroenterology 1998; 114:579.

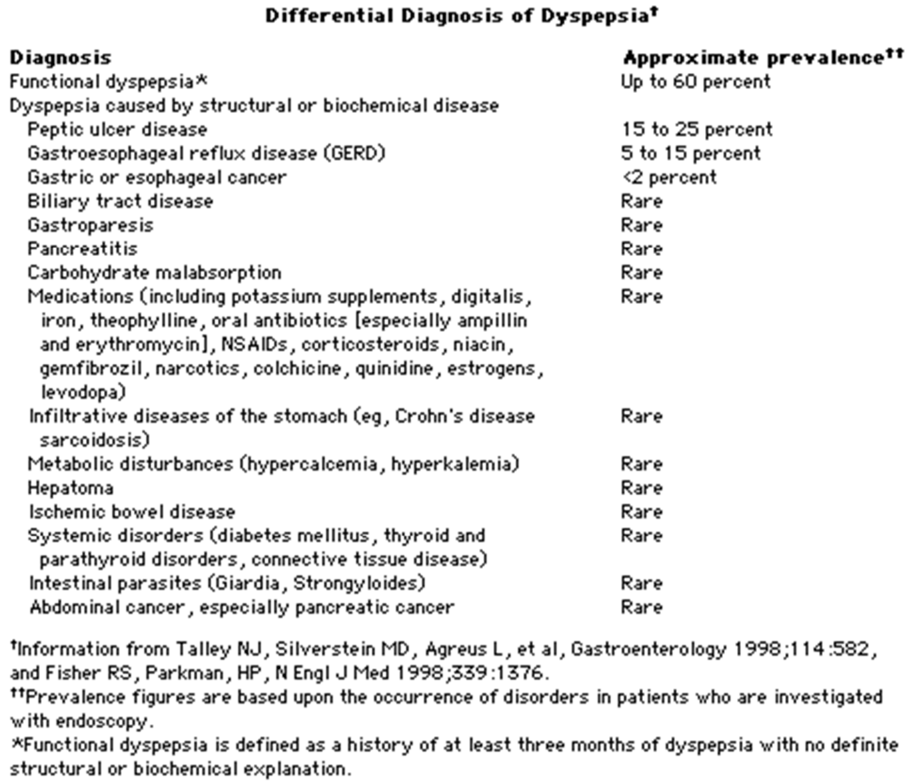
Evaluation of Dyspepsia — Part II†


Endoscopy
Structural diseases including Helicobacter pylori
Functional dyspepsia
Needs a drug trial?
Treat appropriately
Antisecretory or prokinetic*
Follow-up
Evaluate 4 weeks
Success
Failure
Stop drug
Switch to alternate therapy
Success
Failure
Stop drug
Clinically reevaluate
Additional options of uncertain efficacy: Behavioral/psychotherapy Antidepressant

The word 'failure' refers to symptomatic failure.

* Use of the prokinetic cisapride has been severely restricted in the United States because of concerns related to cardiac arrhythmias

† Adapted from American Gastroenterological Association. Medical Position Statement: Evaluation of dyspepsia. Gastroenterology 1998; 114:579.



Differential Diagnosis of Dyspepsia†

Diagnosis	**Approximate prevalence††**
Functional dyspepsia*	Up to 60 percent
Dyspepsia caused by structural or biochemical disease	
Peptic ulcer disease	15 to 25 percent
Gastroesophageal reflux disease (GERD)	5 to 15 percent
Gastric or esophageal cancer	<2 percent
Biliary tract disease	Rare
Gastroparesis	Rare
Pancreatitis	Rare
Carbohydrate malabsorption	Rare
Medications (including potassium supplements, digitalis, iron, theophylline, oral antibiotics [especially ampillin and erythromycin], NSAIDs, corticosteroids, niacin, gemfibrozil, narcotics, colchicine, quinidine, estrogens, levodopa)	Rare
Infiltrative diseases of the stomach (eg, Crohn's disease sarcoidosis)	Rare
Metabolic disturbances (hypercalcemia, hyperkalemia)	Rare
Hepatoma	Rare
Ischemic bowel disease	Rare
Systemic disorders (diabetes mellitus, thyroid and parathyroid disorders, connective tissue disease)	Rare
Intestinal parasites (Giardia, Strongyloides)	Rare
Abdominal cancer, especially pancreatic cancer	Rare

†Information from Talley NJ, Silverstein MD, Agreus L, et al, Gastroenterology 1998;114:582, and Fisher RS, Parkman, HP, N Engl J Med 1998;339:1376.

††Prevalence figures are based upon the occurrence of disorders in patients who are investigated with endoscopy.

*Functional dyspepsia is defined as a history of at least three months of dyspepsia with no definite structural or biochemical explanation.

Malabsorption Syndrome

Definition:

It is a clinical syndrome in which there is malfunction, digestion and absorption of the food intake by the oral route.

Types

A. **Pan malabsorption: Here malabsorption to all nutrient intake.**

B. **Specific Malabsorption: Either malabsorption to an individual nutrient or class of nutrients.**

Physiology of absorption and digestion:

1. **Intraluminal phases:**

- **Fats:** hydrolysis starts at the stomach by gastric lipase.
- Pancreatic lipase digests fats into monoglycerides and fatty acids. The pancreatic lipase requires PH 8 to be active.
- Hyperacidity inactivate the pancreatic lipase.
- Although pancreatic function is required for fat digestion, a person may lose nearly 90% of lipase output from the pancreas before the efficiency of fat digestion and absorption is affected.
- Medium chain triglycerides MCT absorbed directly into portal blood without the need of miceller formation.
- Pancreatic lipase digests TGs into monoglycerides and fatty acids these elements form micelles when combined with bile salts (also important for fat-soluble Vit. Absorption).
- Decreased bile salt concentration may be due to biliary obstruction or liver disease lead to mild steatorrhea.
- Needs colipase – bile salts.
- **Protein:**
    1. Initial breakdown started by gastric pepsins activated by PH 1-3 and inactivated at PH >5.
    2. Then hydrolyzed by pancreatic proteases (trypsin, chymotrp.) into di and tripeptides and amino acids.

3. Additional mucosal brush border oligopeptidases further cleave small peptides, with free amino acids and oligopeptides.

- **CHO:**

- salivary and pancreatic amylases hydrolyze starch into mono and disaccharides.
- The brush border enzymes hydrolyze the disaccharides into monosaccharides (glucose, galactose and fructose.
- Fructose is transported by facilitated diffusion, but glucose and galactose are transported by a sodium-dependent active transporter (SGLT-1).

2. **Mucosal phase:**

- This phase needs sufficient intact area; also intact brush border enzymes
- They are important in the hydrolysis of disaccharides. (Lactase deficiency of the brush border leads to lactose intolerance.)
- This phase lesion is either due to :
    1. Primarily mucosal disease
    2. or resection of part of the intestine.

3. **Absorptive phase:**

lymphatic obstruction leads to impaired chylomicrons and lipoproteins.

Site of absorption of each element:

- Proximal small intestine: fat, iron, and calcium
- Proximal and middle part: CHO, folic acid, other water soluble Vit.
- Middle part: protein,
- Distal: bile salt, Vit. B_{12}
- All intestine and colon: water and electrolytes.

Clinical picture:

CHO: 1. Diarrhea (watery stool duo to osmotic effect of non-absorbed CHO). 2. Weakness 3. Loss of weight 4. Distention duo to fermentation of non-absorbed CHO in the colon by bacteria (gases, bloating). 5. Milk intolerance. 6. Stool PH is acidic <6 and increased stool osmotic gap 7. OGTT, after standard dose of oral glucose ® low rise is an indication of malabsorption. 8. Breath hydrogen test: (if CHO is not absorbed, fermentation by Colonic bacteria into hydrogen as byproduct, exhaled by the lung. So that increased hydrogen in the breath means malabsorption).	**Fats:** 1. Steatorrhea. 2. Watery diarrhea duo to osmotic effect of non absorbed short chain fatty acids. 3. Weight loss 4. Vit A, E, D, K deficiency manifestations. 5. Stool is bulky, greasy, and malodorous and floats. 6. Fecal fat estimation in 72-hour stool collection (diet has 100 g of fat per day several days before stool collection) is diagnostic of fat malabsorption. 7. D-xylose test can be useful to differentiate SB cause from pancreatic insufficiency. 8. D-Xylose is absorbed by SB and excreted in urine. 9. SB cause can be investigated by biopsy, aspiration and radiological images. 10. Pancreatic etiology by: CT, MRCP, ERCP, EUS to evaluate chronic pancreatitis changes. 11. Pancreatic enzymes supplements trial might be diagnostic.
Protein: 1. Edema 2. Weight loss 3. Weakness and fatigue 4. Amenorrhea.	**Water:** 1. Dehydration. 2. Nocturnal urination duo to delayed water absorption.
Mineral and Vit. 1. Night blindness 2. Osteomalacia, bone pains 3. Tetany, paresthesia 4. Glossitis, cheilosis.	**Other symptoms:** 1. Sometimes abdominal pain with the diarrhea 2. Aphthous ulcer (in Celiac disease) 3. Raynaud' s phenomena 4. Anemia (microcytic in iron malabsorption, macrocytic in B_{12} and

5. Cramps. 6. Easy bruising and ecchymotic patches. 7. Pellagra. 8. Sometimes scurvy in severe cases 9. Loss of appetite late in case of depleted vitamins stores.	folate) 5. Lymphopenia (ADIS, lymphangiectasia) 6. Prolonged prothrombin time. 7. Low serum iron, Vit. B_{12}, Carotenes, Ig. 8. **Biochemical estimation:** ***Hypo*calcemia** Poor absorption of calcium or Vit. D. ***Hypo*kalemia** bad absorption and increase loss. ***Hypo*albuminemia** and low BUN ***Hypo*magnesemia.** **Hypophosphatasemia** **Cholesterol and TG** **Alkaline phosphatase**

Causes of Malabsorption:

Impaired digestion: **Primary pancreatic exocrine insufficiency:** Removal Chronic pancreatitis Hemochromatosis Cystic fibrosis Tumor of pancreas. **Gastric surgery (Bliroth, pyloroplasty,Vagotomy)** **Gastrinoma: due to the inactivation of the pancreatic enzymes by the hyperacidity**	**Small intestine abnormalities:** Crohn's disease Amyloidosis Celiac infection Enzyme deficiencies as in lactase deficiency Lymphoma Tropical sprue Whipple's Parasitic diseases Resection of a part (short bowel syndrome), and fistula (jejunoileal fistula)
Reduced bile salt: Bacterial overgrowth Liver disease. Ileal disease and resection.	**Lymphatic obstruction** : e.g. lymphangiectasia and lymphoma. **Drugs**: cholestyramine, neomycin, colchicine, irritant laxative. **Others**: C.H.F, (congestion of the small intestine), carcinoid tumor, diabetes mellitus, adrenal insufficiency, thyroid disorders.

Whipple's disease

Causes:

Chronic infection with ***tropheryma whippleii*** **bacillus**, much system is involved included the small intestine. Its mucosa is infiltrated with macrophages full with periodic acid Schiff (PAS) positive material, with villi distortion.

Clinically

Uncommon disease, due to infection by bacteria, source of infection is unknown, age adults.

A. GIT symptoms: diarrhea, abdominal pain, distention and flatulence.

B. **Other systems:**

- Polyarthritis migratory in nature, peripheral joints.
- Wight loss
- Hypoalbuminemia
- Low grade fever
- Generalized lymphadenopathy
- eye: uveitis, keratitis, retinal hemorrhage
- C.N.S in 10%, dementia, fits, nystagmus, ophthalmoplegia.

Investigations:

- **Histological examination of endoscopic biopsy from the duodenum shows**
  - PAS - positive macrophages that contain gram +ve bacilli.
- **Lymph node biopsy**
- **PCR shows 16 S ribosomal RNA of tropheryma. Whippleii (more sensitive test)**

Treatment

Antibiotic therapy for one year (long duration) e.g. sulfamethoxazole, tetracyclines, ceftriaxone

Celiac disease CD

- CD is characterized by mucosal inflammation, villous atrophy, and crypt hyperplasia, which occur upon exposure to dietary gluten in genetically susceptible individuals and which demonstrate improvement after withdrawal of gluten from the diet.
- It is one of the most common causes of ***chronic*** malabsorption, due to loss of absorptive surface area, reduction of digestive enzymes.

Epidemiology:

- Prevalence now known to be far greater than previously reported due to increasing the diagnosis of silent cases.
- In population based studies, in Caucasians, number ranges between 0.2- 1%.
- In developing countries, the prevalence rates are overlapping European figures:

- 0.53% in Egypt
- 0.79% in Libya
- 0.6% in Tunisia
- 0.88% in Iran
- 0.6% in Turkey

Pathogenesis

Genetic factors:

Celiac disease as an immune disorder that is triggered by an environmental agent (the gliadin component of gluten) in genetically predisposed individuals has a strong hereditary component.

- Strong family predisposition (80% in monozygotic twins). The prevalence in first-degree relatives is approximately 10%.
- High prevalence of celiac in certain chromosomal abnormalities (Down syndrome, Turner syndrome, Williams syndrome).
- A strong association exists between celiac and two human leukocyte antigen (HLA) haplotypes (DQ2 and DQ8). HLA-DQ2 present in 90 to 95% , and HLA-DQ8 in 5% of cases.
- A particular association was found with chromosome 15q26, which contains a type 1 diabetes susceptibility locus.

Environmental factors: (Gliadin reactive T cells)

Tissue transglutaminase is an intracellular enzyme that is released by inflammatory and endothelial cells in response to mechanical irritation or inflammation.

- Gliadin receptor(s) on intestinal epithelial cells may mediate the transport of gliadin peptides to the lamina propria where T-cell activation occurs.
- The driving antigen of the process, gluten, is presented by antigen-presenting cells (APCs) in the lamina propria to CD4$^+$ T cells after it has been deamidated by transglutaminase 2 (TG2).
- Immunoglobulin A (IgA) antibodies are secreted to the gut lumen as secretory IgA (SIgA), and antibodies spill over into the blood.

Clinical presentation

- Celiac dis is not only dis of S.B but it's a multi-organ AI dis.
- It is grossly underdiagnosed, and it has significant complications.
- **Classification:** it may be

<table>
<tr><td colspan="2">Symptomatic</td></tr>
<tr><th>Classical</th><th>Atypical</th></tr>
<tr><td>The classic definition of celiac disease includes the following three features: villous atrophy; symptoms of malabsorption and resolution of the mucosal lesions and symptoms upon withdrawal of gluten-containing foods, usually within a few weeks to months.</td><td>Patients with atypical disease exhibit only minor gastrointestinal complaints. They can display extraintestinal manifestations.

(However, there is a shift from patients presenting with classic celiac disease to more patients with atypical symptoms or an asymptomatic presentation)..</td></tr>
<tr><td colspan="2">Asymptomatic silent or latent (Potential celiac disease).</td></tr>
<tr><th>Silent</th><th>Latent (CD in remission)</th></tr>
<tr><td>No S&S, +ve Ab, Abnormal bx.</td><td>No S&S, +ve Ab, normal bx.</td></tr>
<tr><td colspan="2">Two variants of what has been called latent celiac disease have been identified:

Celiac disease was present before, usually in childhood; the patient recovered completely with a GFD, remaining "silent" even when a normal diet was reintroduced. Approximately 20 percent of such patients continue to have latent disease into adulthood, while the others redevelop variable degrees of villous atrophy. Latency may be transient and thus regular follow-up of such patients is warranted.

A normal mucosa was diagnosed at an earlier occasion while ingesting a normal diet, but CD developed late</td></tr>
</table>

Gastrointestinal (Typical)	Extraintestinal manifestations(Atypical)
▪ ***Diarrhea*** - 45-85% of patients Adult patients with undiagnosed celiac disease rarely present with profuse diarrhea and severe metabolic disturbances (celiac crisis) ▪ ***Flatulence*** - 28% of patients ▪ ***Weight loss*** - 45% of patients; in infants and young children with untreated celiac sprue, failure to thrive and growth retardation are common ▪ ***Weakness*** and ***fatigue*** - 78-80% of patients; usually related to general poor nutrition ▪ ***Severe abdominal pain*** - 34-64% of patients ▪ Anorexia, nausea, vomiting, constipation. ▪ ***Angular stomatitis***, ***angular cheilosis***.	**1- Skin: Dermatitis Herpetiform.** (Symmetric intensely pruritic vesicles, crusts and erosions distributed over the extensor areas of the elbows, knees, buttocks, shoulders and scalp, with a tendency to grouping of individual lesions) **2- musculoskeletal: (metabolic bone dis)** dental enamel hypoplasia, osteopenia, osteoporosis, arthropathy (Nonerosive, polyarticular, symmetrical, large joints), muscle cramps and tetany. **3- hepatobiliary:** hepatic steatosis (elevated transaminase levels), hepatitis, cholangitis. **4- hematological:** Hypersplenism (Prophylactic pneumococcal vaccination has been suggested), iron-deficient anemia resistant to oral iron. **5- cardiac:** carditis, cardiomyopathy. **6- neurological:** peripheral neuropathy, ataxia, fits. **7- psychiatric:** depression, anxiety. (*one third* of pt.) **8- reproductive:** female sub-infertility, recurrent abortions, low birth weight babies. **9- Renal:** *Glomerular IgA deposition* is **common**, occurring in as many as one-third of patients. The great majority of affected patients have no clinical manifestations of renal disease. **10- pulmonary**: Idiopathic pulmonary hemosiderosis also known as Lane-Hamilton syndrome.

Diagnosis of CD

- clinical manifest compatible W dis.
- serological markers.
- SB bx findings.
- clinical response to gluten free diet.
- All testing should be performed while patients are on a gluten-rich diet. No single test can confidently establish the diagnosis of CD in every individual. As a result, the most important initial step in diagnosis is recognition of the many clinical features that can be associated with the disease.

Who should be tested?

- Those with GIT symptoms of malabsorption. This includes patients with symptoms suggestive for IBS or severe lactose intolerance.
- Those without other explanations for extra-GIT signs and symptoms such as iron deficiency anemia, persistent elevation in serum aminotransferases, persistent aphthous stomatitis.
- Patients with type 1 DM, and first-degree relatives of individuals with CD if they have signs, symptoms, or laboratory evidence of possible CD.
- Testing for CD may be considered in asymptomatic first-degree relatives of patients with confirmed diagnosis of CD, particularly children, and in those with Down syndrome.

- Screening of the general population is not recommended. Screening of patients with osteoporosis is also not recommended in the consensus statement.

I- Serological markers:

	SENSITIVITY	**SPECIFICITY**	
1- IgA AGA:	85-90%	90%	(ELISA)
2- IgA EMA:	90%	99.6%	(IF)
3- IgA TTG:	95.1%	98.3%	(ELISA)
4- IgA DGP:	94 %	99 %	
5- IgG DGP:	92 %	100%	

IgA TTG is it's less expensive and the most sensitive and the most frequently used. IgA TTG antibody is the single preferred test for detection of CD in individuals over the age of two years..

if positive confirm with EMA.

- patient on gluten free diet:

Many will come in asking to be tested for CD, but they have already been on a gluten-free diet, so they have set themselves up for a negative test result. That eliminates the sensitivity of detection for celiac disease. Within weeks on a GFD, the antibody response is diminished. If you test patients who have been on GFD for 6-12 months, approximately 80% of people will lose their antibody response.

Therefore, when you are considering celiac disease, take a good dietary history before you embark on serologic testing. The results can be misleading. The same is true for biopsies, which will also change on a GFD.

II- HLA typing:

- The **HLA-DQ2 and -DQ8** genotypes are abnormally in virtually all patients with celiac disease. The HLA-DQ2 test picks up 95%, and the HLA-DQ8 another 5% of patients. The negative predictive value for both tests is higher than 99%.
- The problem with this test -- and the reason we don't test everybody with this genetic test -- is that 25%-30% of the white population of the United States will test positive, but they don't have celiac disease.

III- UGIE AND BX.

Confirmatory testing is done through *duodenal biopsies*.

***Who* should undergo duodenal bx?**

1- positive screening Ab test and patients with a high probability of CD (>5 percent), regardless of the serology, should undergo an UGIE with small bowel biopsy to confirm the diagnosis of CD. (Exceptions are those who have biopsy-proven DH in whom the diagnosis can be established without a small bowel biopsy).

2- Early osteoporosis or bone fracture.

3- unexplained iron def. anemia.

4- Neuropathy or ataxia.

Biopsies are assessed according to histologic criteria, which include the **Marsh-**Oberhuber criteria and the Corazza criteria. The Corazza criteria are probably the most current, but many of us are more familiar with the Marsh criteria.

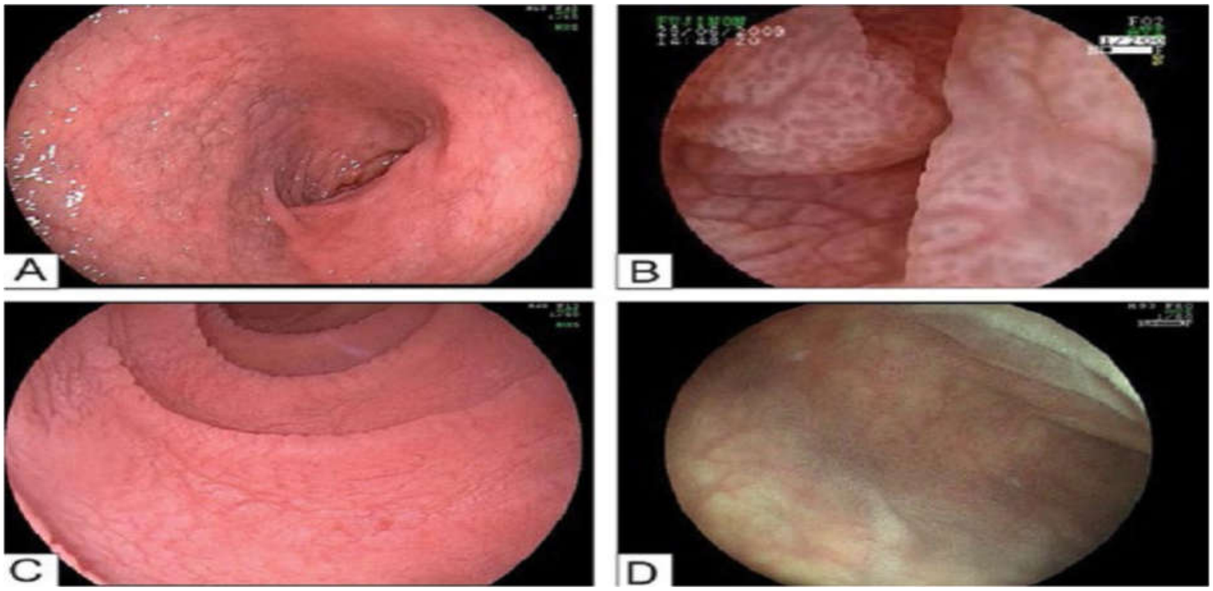


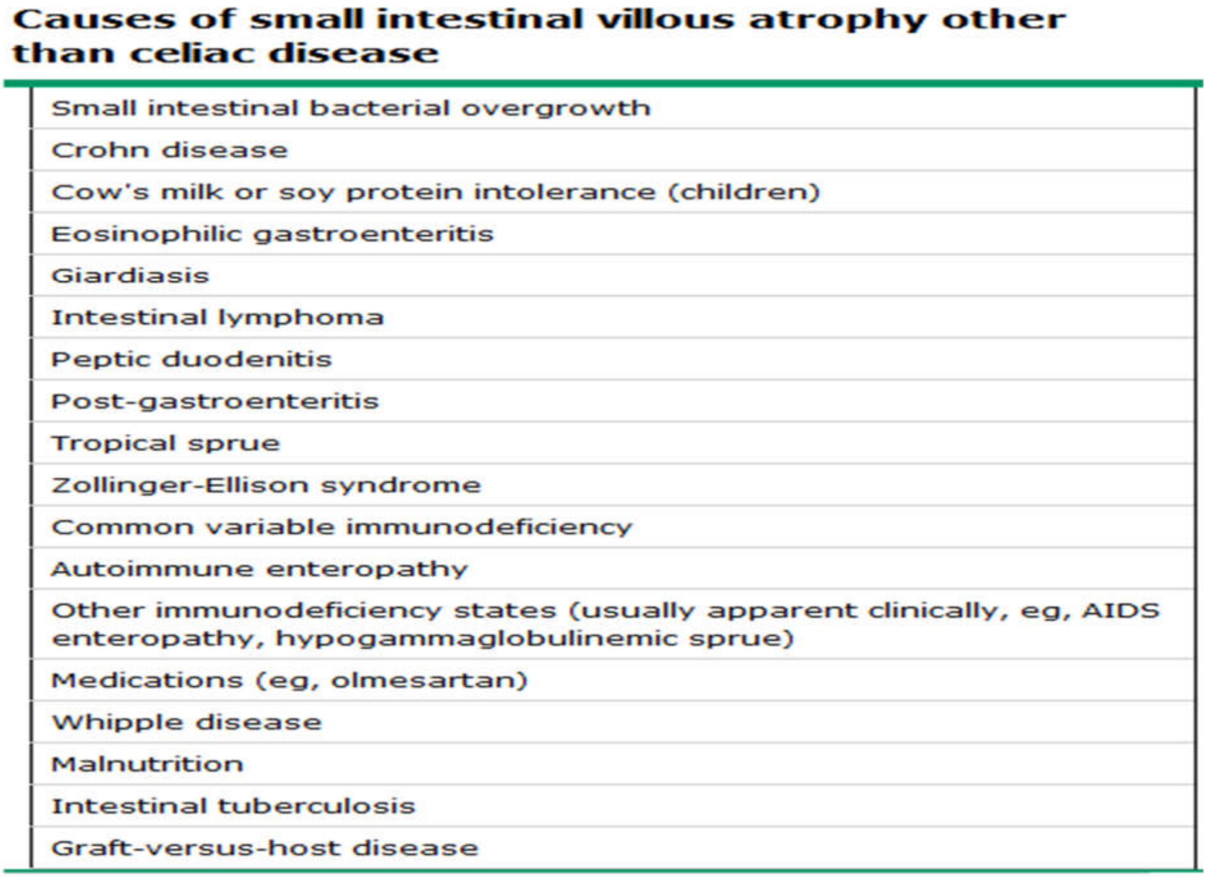
FIGURE 1.

A: Duodenal bulb, mucosal nodularity/mosaic pattern;

B: Total villous atrophy; water- immersion technique with magnification;

C: Second portion of the duodenum; water-immersion technique, mucosal fissures and scalloping of folds;

D: Areas of total villous atrophy interspersed with areas of partial villous atrophy (patchy villous atrophy



Causes of small intestinal villous atrophy other than celiac disease

Small intestinal bacterial overgrowth
Crohn disease
Cow's milk or soy protein intolerance (children)
Eosinophilic gastroenteritis
Giardiasis
Intestinal lymphoma
Peptic duodenitis
Post-gastroenteritis
Tropical sprue
Zollinger-Ellison syndrome
Common variable immunodeficiency
Autoimmune enteropathy
Other immunodeficiency states (usually apparent clinically, eg, AIDS enteropathy, hypogammaglobulinemic sprue)
Medications (eg, olmesartan)
Whipple disease
Malnutrition
Intestinal tuberculosis
Graft-versus-host disease

Histological criteria:

The established celiac lesion shows typical morphological features including:

1-Increased numbers of intraepithelial lymphocytes (IELs).

2-Decreased enterocyte height,

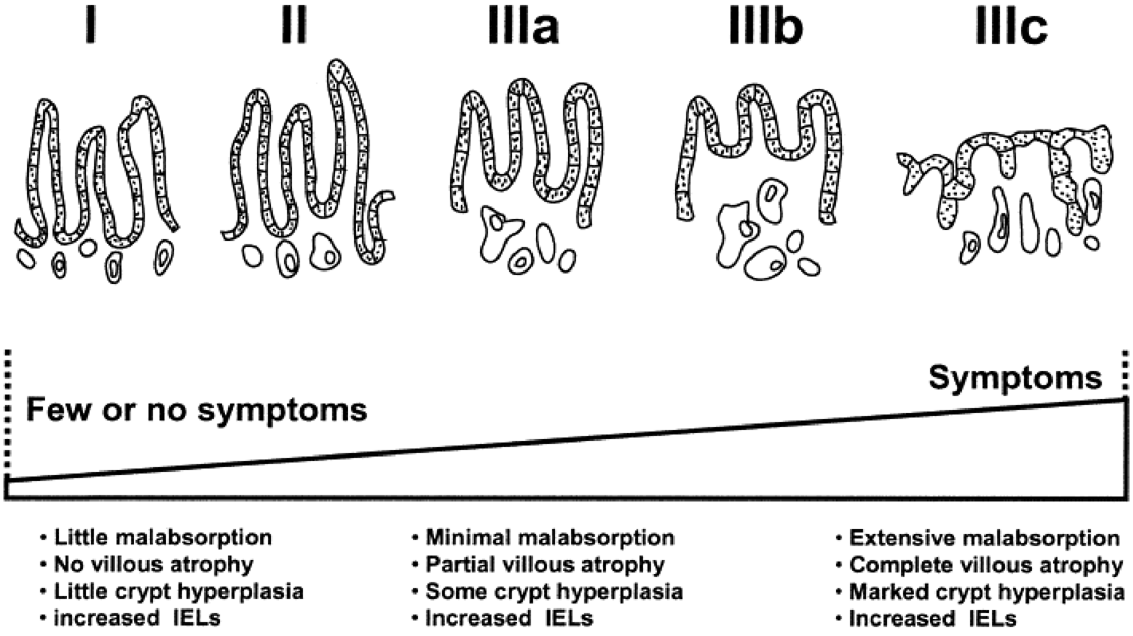
3-Villous atrophy.

4-Crypt hyperplasia.

The severity of histologic changes in the small bowel does not necessarily correlate with the severity of clinical manifestations. Although there is a gradient of decreasing severity from the proximal to the distal small intestine, correlating with the higher proximal concentration of dietary gluten.

Quantitative histology (villous height, crypt depth, density of IELs per 100 enterocytes) provides the most sensitive and accurate method to monitor disease activity over time.

- **Modified Marsh Classification**



Upper endoscopy with at least 6 duodenal biopsies is considered the criterion standard to help establish a diagnosis of celiac disease.

Marsh's classification is the histological classification system of CD most widespread and used worldwide, both for diagnostic purposes and for histological reevaluation after institution of gluten-free diet.

duodenal biopsies **can be graded into the following *5* stages:**

Stage 0	**Normal**
Stage 1	**Increased percentage of intraepithelial lymphocytes (>30%)**
Stage 2	**Increased presence of inflammatory cells and crypt cell proliferation with preserved villous architecture**
Stage 3	**Mild (A), moderate (B), and subtotal to total (C) villous atrophy**
Stage 4	**Total mucosal hypoplasia**

Treatment:

1. **Gluten free diet.**
2. **Because lactase deficiency is commonly associated avoid milk products.**
3. **Vitamins, calcium, iron, help in the start phase of therapy to enhance improvement.**
4. **Patients with latent CD are currently not advised to be on a GFD but should continue to be monitored and rebiopsied if symptoms develop. However, it is important that such patients are evaluated with multiple intestinal biopsies since histologic abnormalities can be patchy.**
5. **Recently immunosuppress. Steroids in refractory celiac.**

Tropical sprue

This is due to overgrowth of Coliforms in the jejunum with enterotoxin production

Leading to villous atrophy with Malabsorption syndrome.

Treatment:

- **2 months antibiotic therapy (tetracycline 250 mg/ 6 hours)**
- **Folic acid and B_{12}.**

Bacterial overgrowth

a.k.a *Stasis syndrome* a.k.a *Blind loop syndrome*

- **Overgrowth of bacteria within the small intestine leads to Malabsorption.**
- **Normally the small intestine may have very small number of bacteria if this number increase to give malabsorption this syndrome is present**

- **Clearing mechanism of organisms in the small intestine:**
  - **Motility.**
  - **Gastric acid secretion.**
  - **Luminal immunoglobulin.**

Mechanism of malabsorption:

1. **Deconjugation of bile salt by bacteria**

2. **Bacteria produce toxic products, lead to mucosal damage.**

3. **Malabsorption of CHO and bile acid increase their level in the colon, leads to diarrhea**

4. **Bacteria itself take essential elements from the intestine leading to malabsorption of some nutrients such as Vit. B_{12}.**

5. **Disturbed CHO metabolism by gram -ve aerobes.**

Causes of this syndrome:

(gastric causes, pancreatic causes, small intestine causes, Colon causes):

1. **Hypo or achlorhydria**
2. **Chronic Pancreatitis**
3. **Small intestinal: Bliroth II, diverticulosis, surgical blind loop syndrome.**
4. **Fistula in the small intestine as in Crohn's disease, Hypogammaglobulinemia.**
5. **Motility disorder such as in diabetes, systemic sclerosis.**
6. **Pseudo obstruction of the small intestine**
7. **Colonic anomalies with the small intestine or resection of the ileocecal valve**

Symptoms:

1. **As that of malabsorption (distention, diarrhea, loss of weigh, anemia)**
2. **History of the cause if present**

Diagnosis:

- **Test of malabsorption.**
- **Take sample from the upper part of the intestine by a tube for culture, Organisms >100,000/mI is positive (gold standard).**
- **C13, C14 Xylose absorption test and detect isotopes in the breath. (collect CO_2 with C14 or C13 in the breath as the bacteria split xylose and release CO_2)**

Treatment:

1. **Antibiotics (cephalosporins or tetracycline) for 10 days.**
2. **Octreotide to stimulate motility.**
3. **Other nutritional therapy.**

Small intestinal tumors:

They less common, they are benign or malignant.

In general symptoms are:

1. **Vague abdominal pain**
2. **Bleeding**
3. **Intestinal obstruction**
4. **Melena**
5. **Anemia & Specific symptoms such as carcinoid syndrome.**
6. **No symptoms**

Types:

1. **Benign are usually asymptomatic unless bleeding occurs. Adenoma, lipoma, leiomyoma**
2. **Malignant:**
    - **Adenocarcinoma: ampulla's of Vater is the common site**
    - **Sarcoma : leiomyosarcoma, Kaposi's.**

    They presented with - Bleedings - Metastasis - Obstruction

Short Bowel Syndrome:

- **it is either absolute or relative.**
- **It depends upon the length lost from intestine, site of resection or lost, and integrity of the rest of the intestines.**
- **The jejunum function can be all performed by ileum if intact but the reverse is not true.**
- **The TI if lost affects vit.B12 deficiency and bile salts malabsorption leads to steatorrhea.**
- **Calcium oxalate stones occur if the colon is intact.**
- **Causes might be congenital or acquired.**
- **Congenital as in midgut volvulus, omphalocele, JI atresia, or congenital short bowel.**
- **Acquired as in surgical resection of part of the intestine, intestinal ischemia, radiation enteritis, or crohn's enteritis.**

Management

- *Nutritional* **therapy**
  - **a. Enteral nutrition.**
  - **b. Parenteral nutrition.**
- *Specific* **Treatments for Malabsorption Disorders**

Celiac sprue	Gluten-free diet
Tropical sprue	Folate, B12, tetracycline
Collagenous sprue	Steroids
Whipple's disease	Penicillin G, streptomycin, TMP/SMX
Lactase deficiency	Lactase supplementation
Other disaccharidase deficiencies	Dietary restriction
Bacterial overgrowth	Rotating antibiotics
Abetalipoproteinemia	Low-fat diet and fat-soluble vitamin supplementation
Lymphangiectasia	Correct causative disease, MCT
Crohn's disease	Steroids, 5-aminosalicylates
Eosinophilic enteritis	Steroids, cromolyn
Amyloidosis	Correct underlying process
Pancreatic insufficiency	Pancreatic enzymes
Short bowel syndrome	Medium-chain triglycerides, low-oxalate diet, TPN, PPI, GH, GLP-1
Giardia	Metronidazole, quinacrine
Isospora belli	TMP/SMX
Diphyllobothrium latum	Praziquantel
Strongyloidiasis stercoralis	Thiabendazole

GIT motility disorders & functional colonic disorders

- ***Function of the GIT as a digestive organ depends on three distinct mechanisms working in harmony namely: secretion, motility and absorption.***
- ***It has been estimated that problems of motility may account for about 50% of gastroenterologist's clinical care load.***
- ***Many of the underlying mechanisms controlling the motility of the gut are not fully understood. However, recent advances in diagnostic methodology and electrophysiologic measurements of the gut's activities have provided new insights.***

Function of the Esophagus:

1. ***Transfer function.***
2. ***Anti-reflux function.***

Types of Esophageal Peristalsis:

1. ***Primary (swallow-induced) Peristalsis.***
2. ***Secondary (distention-induced) Peristalsis.***

Pressure Measurements of the *normal* Esophagus:

UES	***Resting pressure = 100 mmHg*** ***pressure during relaxation = Zero or below***
Body of the Esophagus	***Resting pressure = -5 mmHg*** ***Pressure during contraction = 3o-180 mmHg***
LES	***Resting pressure = 20-40 mmHg*** ***Pressure during relaxation = 5 mmHg***
Gastric fundal pressure	***= 5 mmHg***

Manometric Criteria of *Normal* Esophageal Contractions:

1. ***Sequential or peristaltic from above downwards.***
2. ***Amplitude of 30-180 mmHg.***
3. ***Duration of 2-6 seconds.***
4. ***Single and occasionally double peaked.***

Manometric Classification of Esophageal Motility *Disorders*:

I) Abnormalities of esophageal peristalsis	II) Abnormalities of LES resting pressure
1. Diffuse esophageal spasm (DES). 2. Nutcracker esophagus. 3. Non-specific esophageal motility disorders (NEMD). 4. Aperistaltic esophagus.	1. Hypertensive LES. 2. Hypotensive LES (PSS).
III) Abnormalities of LES relaxation	**IV) Abnormalities of UES relaxation**
1. Incomplete relaxation (achalasia). 2. Spontaneous relaxation (GERD).	1. Primary achalasia of cricopharyngeal. 2. Secondary relaxation failure due to systemic neurological diseases.

Clinical Presentations of Esophageal Motility Disorders:

1. Asymptomatic cases.
2. Cases dominated by pain.
3. Cases dominated by dysphagia.
4. Complicated cases.

Protocol of Investigations:

1. Cardiac assessment.
2. Radiology (Barium swallow and meal).
3. Upper endoscopy.
4. Esophageal manometry and/or prolonged ambulatory pH monitoring.

Treatment:

***I) Defective transport function*:** 1. Reassurance**.**
2. Pharmacologic therapy a) Nitrates. b) Calcium-channel blockers.
3. Pneumatic dilatation. 4. Esophago-cardio myotomy.

II) Defective anti-reflux function: 1. Reassurance. a) Anti-secretory drugs b) Prokinetic.
2. Anti-reflux surgery.

GI Transit:

Regulated smooth muscle contractions results in coordinated changes in gut intra-luminal pressure, which controls the transit of chyme through the GIT . Each of the major sections of the GIT has a specific function that requires a different transit pattern.

A pressure amplitude gradient, rather than a frequency gradient, that determines the transit for each part of the GIT.

Circular contractions segment the lumen, mixing the contents to expose the mucosa to continually different contents.

The longitudinal muscle shortens the bowel, moving intraluminal contents forwards.

The motor migratory complex (MMC)

Consists of three different phases.

Phase 1*: is a period of inactivity.*

Phase 2*: is a period of intermittent phasic contraction similar to the post prandial pattern.*

phase 3*: is a continuous period of contractions which are at slow wave frequency, specific for that region of the bowel.*

- Sphincters are high-pressure zones interposed through the GIT.
- Contraction or relaxation of the sphincters is controlled by enteric neurotransmitters or, by circulating peptide hormones, in response to changes in pressure of the surrounding bowel, or physiologic stimuli.
- Proximal distention relaxes all sphincters; while distal distention contracts sphincters.

Pathogenesis of *colonic* motility disorders:

Slow transit	Rapid transit
1) Increased segmenting contractions . Primary constipation. . Irritable bowel syndrome (spastic). . Diverticular disease. . Anal outlet obstruction. Congenital (segmenting – Hirschsprung disease). ***2) Decreased segmenting contractions.*** . Irritable bowel syndrome (inertia). . Primary colonic pseudo – obstruction. . Diabetes mellitus. . Progressive systemic sclerosis. . Spinal cord injury.	Functional diarrhea. Bile salt diarrhea. Surreptitious abuse of laxative.

Gastric motility disorders:

Delayed gastric emptying	***Rapid*** gastric emptying
1. Post vagotomy.	1. Dumping syndrome.
2. Diabetes mellitus.	2. Pancreatic insufficiency.
3. Viral infections.	3. Celiac sprue.
4. Reflux esophagitis.	4. Zollinger – Ellison syndrome.
5. Brain stem lesions.	5. Duodenal ulcer.
6. Anorexia nervosa.	6.Tachygastria.

Small intestinal motility disorders:

Decreased motility	***Increased*** or uncoordinated motility
1. Hollow visceral myopathy (primary intestinal pseudo – obstruction). 2. progressive dystrophy. 3. Hypothyroidism. 4. Jejunal diverticulosis, Jejunal bypass.	1. Primary visceral neuropathy. 2. Carcinoma-associated visceral neuropathy. 3. Progressive systemic sclerosis. 4. Irritable bowel syndrome. 5. Diabetes mellitus. 6. Infectious diarrhea. 7. Mass lesion of brain stem. 8. Amyloidosis. 9. Hyperthyroidism. 10. Carcinoid syndrome. 11. shy – Drager syndrome.

Inflammatory Bowel disorders

It includes two distinct chronic idiopathic destructive inflammatory diseases of the gastro intestinal tract that typically manifest during late **childhood** and **adolescence**:

1- Crohn's disease

2- Ulcerative colitis

Epidemiology:

A. incidence: in US▶ **Crohn's: 5/100,000 UC: 15/100,000**

B. Most of cases are ***bimodal*** ▶ **Between: 15-40 y** & **50-80 y**

C. Race: • More in Jews (4 folds) • More in whites and well developed areas

Pathophysiology of IBD

Immunologic factors: gut flora

1. IBD is referred to as an autoimmune disease or disorder
2. There is an enhanced level of lamina propria T cell activation.
3. Increased expression of surface markers of T cell activation.
4. Increased production of T cell lymphokines.
5. Increased cytotoxic T cell function.
6. This enhanced T cell activation leads to the recruitment of effector cells such as neutrophils and the subsequent elaboration of destructive substances such as proteases & reactive O2 metabolites. The immune mechanism is not directed against self-antigen.
7. The trigger for T cell activation in IBD is unknown. Now gut flora changes considered +ve main trigger.
8. Some theories accuse chronic mycobacterial infection as the underlying cause of Crohn's disease.
9. The defect in immune system in IBD is thought to be multifactorial.
   •Exogenous antigen
   •Enhanced delivery of antigen i.e. increased intestinal permeability.
   •A heritable propensity to mucosal immune dysregulation.

10. 60-70% of patients with UC has antineutrophil cytoplasmic antibody P-ANCA usually it is associated with HLA-DR2 allele.

11. ASCA antisaccharomyces cervicae antibody is seen in over 60% of patients with Gohn's disease & in < 10% in UC. It becomes positive when intestinal permeability is increased.

Genetic factors

1st degree relative in Crohn's disease is 5-8% in ulcerative colitis 2-5%.
IBD local: IBD1 ➔ IBD8 [imp IBD1 ➔ Chr 16 (CD)]

Environmental factors

IBD is higher in urban than rural areas.
Higher levels in higher socioeconomic classes.
Increase risk of IBD among users of oral contraceptives.
Decreased risk of UC among smokers while in Crohn's disease there is an increased risk of the disease.

CROHN'S DISEASE

Crohn's is the name of the doctor who first described the disease in US in 1932.

What is Crohn's disease

1. **It is one of IBD**
2. **non specific inflammation of any segment of GIT.**
3. **Discontinuous or skip area**
4. **Granulomatous, ulceration fissuring or transmural inflammation**

Synonym

- **regional enteritis**
- **Regional ileitis**
- **Granulomatous colitis**
- **Granulomatous enteritis**

Location = site

Ileocecal 40-50%

- **small intestine 30-40**
- **colon only 20%**
- **other areas involvement are rare it may involve anal canal in 1/3 off cases but usually with rectal sparing.**

Pathology:

Gross **pathology**

1. **Thickened, edematous mesentery of involved part.**
2. **Adipose tissue from the mesentery may be seen to spread over the serosal surface of the bowel (creeping fat).**
3. **Bowel loops adhered together or to adjacent structures.**
4. **Mucosal lesions begins as aphthous ulcer.**
5. **Ulcers enlarge, deepen, coalesce to form transverse and longitudinal linear ulcers.**
6. **Cobble stone appearance ulcers may penetrate to form fistula and or abscess.**
7. **Healing occurs by fibrosis → stricture formation.**

MP

Transmural inflammation and the patchiness of inflammatory infiltrate.

Non necrotizing granulomatous are characteristic (its absence does not exclude the disease.

Clinical picture

1. Remission and relapses sometimes persistent symptoms
2. Three categories (one of them according to behavior) inflammatory, fibro stenotic, fistulizing.
3. Classic symptoms colicky right abdominal pain (lower quadrant), diarrhea.
4. Low grade fever & weight loss high fever → abscess formation
5. Hematochezia occur rarely and with colonic involvement.

Signs:

1. Tenderness all over the abdomen specially right iliac fossa
2. Palpable mass may be present either thickened and adherent loops or abscess.
3. PR: perirectal abscess, fistula. Rectal prolapse, fissure,
4. Patient with inflammatory type malabsorption and weight loss, fibro stenotic → partial intestinal obstruction pain, vomiting, bloating, fistulizing→ profuse diarrhea fistula may open to the skin or open in the urinary bladder→ pneumaturia and UTI

Diagnosis:

Diagnosis depend on clinical, radiologic endoscopic, histologic finding. ASCA is not diagnostic alone but confirms other criteria.

I. Laboratory findings

Leuko***cytosis***, Thrombo***cytosis***, ***Anemia***: *(Fe decrease, anemia of chronic disease)*

ESR & **CRP** increase

Hypoalbuminemia , **B12 deficiency**

Stool analysis; leucocytes.

Serology: *PNACA*: 60% UC ***ASCA*** +ve: 60% CD

Specific stool test: -Fecal calprotectin -Fecal lactoferrin

II. Imaging studies:

1. **Barium follow through** features: skip lesions, cobble stoning luminal narrowing, string sign.
2. **Barium enema** is inferior to colonoscopy to evaluate the extent of mucosal involvement of the colon.

Reflux of barium into the terminal ileum may provide documentation of ileal disease which differentiate crohns disease from UC.

3. **CT** enter **colonography** for diagnosis + to diagnose complication (abscess or enter vesicular fistulas).
4. **Plain x-ray** for:
    - Intestinal obstruction
    - Toxic megacolon

III.Radiological features of major forms of IBD

Features	**Ulcerative Colitis**	**Crohn's Disease**
Radiologic findings	**Continuous**	**Discontinuous, segmented**
• **Distribution**	**Fine, superficial**	**Deep, with submucosal extension**
• **Ulceration**	**Absent**	**Common**
• **Fissures**	**Rare**	**Common**
• **Strictures or fistulas**	**Dilated ("backwash ileitis")**	**Narrowed, nodular**
• **Ileal involvement**		

III. Endoscopy:

1. **Colonoscopy:**
    - **procedure of choice for evaluating the presence and extent of crohn's dis. It also allows for intubation of terminal ileum.**
    - **Biopsy is taken from normal and diseased areas.**
    - **Linear ulcers, cobble stone appearance rectal sparing.**
2. **UGIE if needed.**
3. **Video capsule endoscopy.**

Endoscopic features of major forms of IBD

Features	Ulcerative Colitis	Crohn's Disease
Endoscopic findings	**Very common**	**Fairly common**
• **Friability**	**Absent**	**Common**
• **Aphthous and linear ulcers**	**Absent**	**Common**
• **Cobblestone appearance**	**Common**	**Fairly common**
• **Pseudo polyps**	**Very common**	**Fairly common**
• **Rectal involvement**		

Pathological changes associated with Crohn's disease and ulcerative colitis

Crohn's disease	Ulcerative Colitis
• Rectal sparing and skip lesions	• Continuous distal disease
• Mucin retention	• Mucin depletion
• Histiocytic aggregation	• Basal plasma cytosis
• Focal mucosal injury	• Diffuse mucosal atrophy
• Sarcoid-like granulomata	• No granulomata
• Anal involvement	• Anal sparing

DD:

Ileocecal crohn's

1. UC
2. Acute appendicitis
3. Caecal diverticulitis
4. Pelvic inflammatory disease
5. Ileocecal TB
6. Cytomegalovirus
7. Ectopic pregnancy
8. Vasculitis
9. Lymphoma.

Complications:

1.Abscesses

2.Fistulas

3.Stricture

a. Acute inflammation and edema.
b. Compression by a mass (abscess)
c. Adhesion
d. Fibro stenotic stricture.

4.Perianal disease: fistula, abscess

5.Nutritiional decrease: loss of B12, Bile acids → fat malabsorption, oxalate stones.

6.Cancer: small bowel adenocarcinoma, cancer colon-no risk.

CD colitis = UC

Treatment

1. **5-amino salicylic acid (5-ASA)**

A. sulfasalazine is 5-ASA + sulfa pyridine. When taken orally 5-ASA is released in the colon by the action of bacteria mechanism of action is inhibition of interleukin I production and scavenging of free O2 radicals.

B. Sulfa-free oral mesalamine (mesalamine, olsalazine, balsalazine)

- Dose 4g/day for mild & moderate it has little effect on small bowel crohn's dis.
- Sides effect nausea, vomiting, headache rash, fever, if happened build up the dose.
- Also, motility sperm disorders other compounds contain 5-ASA only to decrease side effects (mesalamine).

C. Others sustained release formula, tablets, supp. & enema are available.

2. **Corticosteroids**

Action: Act through impairment of T cell function and impairment of phagocytosis and chemotaxis and cytokine production.
Dose: 40-60 mg prednisone/day

in severely ill, patients:
- should be hospitalized.
- IV methyl prednisolone 60-100 mg/day once remission occurs start tapering the dose.

Side effects: weight gain, acne, hypertension, DM, infection, osteoporosis
• **Local** acting steroid: budesonide, no systemic SE

3. **Immunosuppressive drugs**:

- azathioprine 50gm TDS. **6-mercaptopurine methotrexate**, **cyclosporine**

= CBC is done monthly for liability of bone marrow suppression.

4. **Biological**: Anti-TNFa: Infliximab (Remicade)

Indications: severe cases Failure of conventional treatment Steroid dependent

Dose: 5 mg/kg bwt

Induction at 0, 2, 6 ws ***Maintenance***: at 8 ws interval

S.E.: -Allergic reaction - Flaring of T.B.

5. **Antibiotics:**

- metronidazole is the best in ***colonic*** and ***ileocolonic*** type.

6. **Nutrition**

- B12, Ca, Mg. in fistula: Stop oral feeding for some time fibro-stenotic → low residue diet

7. **Treatment of *complications*.**

a- Perforating disease abscess → surgery broad spectrum antibiotics drainage if possible under guidance of CT.

b- Fistula: Remicade injection it is antitumor necrosis factor alpha 5 mg/kg 0,2,6 weeks.

c- fibro stenotic → obstructive symptoms bowel rest, nasogastric suction hydration. Aggressive medical therapy if no response→ surgery.

d- Perirectal disease metronidazole 1st corticosteroids + 6 mercaptopurine surgery or remicade.

Ulcerative Colitis

Sudden acute diarrhea (blood + mucus) not responding to usual treatment, we have to exclude infectious diarrhea, definite diagnosis is by colonoscopy and biopsy.

Pathology: NEA

1. Erythema, edema.
2. Begins in the rectum and ascends.
3. Sharp line of demarcation between healthy and unhealthy.
4. Inflammatory polyps or pseudo-polyps.
5. Loss of haustration, flat appearance.
6. In extremely ill toxic megacolon (colonoscopy is contraindicated & Ba enema is also contraindicated).

MP:

Crypt abscess neutrophils in lamina propria, inflammatory process does not disrupt muscularis mucosa.

Clinical picture

1. Dysentery Rectum is almost always involved.
2. Extent: may be
    - pancolitis 30%
    - 30-40% is limited to rectosigmoid.
    - 30% lt sided colitis
    - The rest is intermediate.
3. Fever, tenderness, anemia, albumin decrease.
4. Some patients complain of diarrhea alone or blood/ rectum alone.
5. 15-25% → extracolonic manifestation.

Ulcerative Colitis in Montreal 2005

Extent		Anatomy
E1	Ulcerative proctitis	Involvement limited to the rectum (that is, proximal extent of inflammation is distal to the rectosigmoid junction)
E2	Left sided UC (distal UC)	Involvement limited to a proportion of the colorectum distal to the splenic flexure
E3	Extensive UC (pancolitis)	Involvement extends proximal to the splenic flexure.

Severity of UC

Severity		Anatomy
S0	Clinical remission	Asymptomatic
S1	Mild UC	Passage of four or fewer stools/day (with or without blood), absence of any systemic illness, and normal inflammatory markers (ESR)
S2	Moderate UC	Passage of more than four stools per day but with minimal signs of systemic toxicity
S3	Severe UC	Passage of at least six bloody stools daily, pulse rate of at least 90 beats per minute, temperature of at least 37.5ºC, hemoglobin of less than 10.5 g/100 ml, and ESR of at least 30 mm/h

	UC rare	**Crohn's disease common 1/3**
1- Perianal disease	Rare	Common 1/3
2- Fistulas	Rare	Common in 40%
3- Abscess	Rare	20%
4- Stricture	Rare	Common
5- Rectal involvement	Always	Spared
6- Iteal involvement	Rare	75%
7- Inflammation	Mucosal	transmiural
8- Granuulomas	Rare	20%

Intestinal **complications**	***Extra*** **-intestinal manifestations**
- Patients with ***toxic megacolon*** present with fever, tachycardia 120/min abdominal distension, localized peritonitis dilated colon on plain X-ray leucocytic count > 11,000 no Ba enema, no colonoscopy. - ***Perforation***: severe colitis → perforation (mostly in sigmoid colon) high mortality rate. - ***Stricture*** it is uncommon if present suspect malignancy. - ***Massive hemorrhage*** if uncontrollable treatment is by colectomy. - ***Cancer*** is related positively to the duration and the extent of the colon involvement colonoscopy every year if dysplasia is present → colectomy	**A-Reactive arthropathy** 1. Strongly associated with the extent of colonic involvement (colitic arthritis). 2. Resolves with treatment of underlying bowel disease. 3. It is asymmetric, migratory 4. Sacroiliitis is the most common axial arthritis. 5. Ankylosing spondylitis is 30 times more common in IBD 6. **HLA-B27** +ve in >90%. **B- Oral manifestations** ▪ Aphthous ulcers in **crohn's** disease. ▪ Hypertrophy of lips; **crohn's** disease. **C- Ocular manifestations** ▪ Scleritis and uveitis (anterior) episcleritis with acute active disease usually associated with erythema nodosum and HLA-B27. **D- hepatobiliary** ▪ ***1ry sclerosing cholangitis*** [**PSC**]; specially with UC its incidence is unaffected by colectomy. ▪ **Peri-cholangitis** increase alkaline phosphatase and transaminases. ▪ **Cholesterol gall stones** in ileal disease due to decrease in bile salt pool. **E-Dermatologic manifestations** erythema nodosum in **crohn's**, pyoderma gangrenosum in **UC**. **F-lung disease** (*least common*) *asymptomatic* decrease in diffusing capacity to disabling bronchiectasis.

Treatment of UC:

I. ***Sulfasalazine*** remains the *drug of choice* 2-4 grams we use it alone with **local** treatment in *mild* and *moderate* disease

***mild* < 4 motions / day**

- in ***moderate*** we use also; **5 ASA enema** and **suppository** and **hydrocortisone enema**,

2 weeks before accepting failure of treatment.

***Moderate* disease 4-6 motions/ day**.

II. Corticosteroids

- If no response we start ***oral*** cortisone 40-60mg for 3-4 weeks to attain *remission* then start withdrawal fluids.

- **IV** with ***prednisolone*** 60-100 mg/day and nutritional support in ***severally ill*** patients.

- ***Budesonide*** 4-8 mg daily, cortisone acting locally in intestine-no or little systemic actions.

III. Immuno-suppression

if patient becomes cortisone dependent or refractory to treatment the same as in crhon’s dis.

IV. Biological treatment:

Infliximab be sure that the patient. Has no active TB.

V. Colectomy total with ileal pouch

Treatment of *toxic megacolon*

1. Stop oral feeding
2. Hospitalize the patient
3. Fluid and electrolyte balance
4. Broad spectrum antibiotics
5. Methyl prednisolone 100 mg/ day
6. If no improvement within 48 hours → colectomy.
7. If rupture → air under the diaphragm, peritoneal signs on abdomen → surgery.

Prevention of relapse 5 ASA

Surgery in *UC*	**Surgery in *Crohn's* disease**
1. Massive hemorrhage 2. Perforation 3. Fulminant colitis (Biological). 4. No response to treatment (biological). 5. Higher dose cortisone dependent (biological) 6. Dysplasia or malignancy 7. Toxic megacolon.	1. Strictures: balloon dilation or reconstruction. 2. Fistulas (trial first with infliximab 3. Mass or abscess. 4. Intestinal obstruction not responding to medical treatment

Gastrointestinal Tumors

Esophageal tumors

- **5 % of all GI tumors**
- **Mean age at diagnosis 60 years**
- **Types:**

the two most common malignant types are:

1-Squamous cell carcinoma

- **Incidence and epidemiology**
- **Most common malignant tumor of the esophagus**
- **Male : female 3:1**
- **Commonest site in mid esophagus**
- **Etiology and pathogenesis**

Environmental risk factors

- **Tobacco Smoking**
- **Vitamin deficiencies (A, C, E, B12, folic acid)**
- **Trace elements deficiencies (selenium, zinc, molybdinum)**
- **i.e. poor consumption of green and yellow vegetables**

Others

- **Achalasia of the cardia**
- **Ionizing radiation**
- **Cancers of head and neck**
- **Tylosis (autosomal dominant, hyperkeratosis)**
- **Plummer Vinson syndrome**

1- Adenocarcinoma of the esophagus

- **Incidence and epidemiology**
- **Increasing in U.S. by 20 % every year**

- **Higher incidence in U.K. Australia, Holland**
- **White males > 40 year**
- **Common in distal esophagus**

➢ **Risk factors:**

- **obesity BMI >30 versus <22 risk 17 folds**
- **reflux disease and Barrett,**
- **diet**
- **smoking**
- **scleroderma**

Esophageal *adeno-carcinoma* and *reflux* disease

- Frequent symptoms of reflux is associated with increased risk

- Presence of Barrett's esophagus (intestinal metaplasia with specialized columnar epithelium) is the most important risk factor

Endoscopic *surveillance* of *Barrett's* esophagus

According to the ACG 2016

Screening for BE may be considered in men with chronic (>5 years) and/or frequent (weekly or more) symptoms of gastroesophageal reflux (heartburn or acid regurgitation) and two or more risk factors for BE or EAC.

These *risk factors* include:

- **age >50 years, Caucasian race,**
- **presence of central obesity (waist circumference >102 cm or waist–hip ratio (WHR) >0.9),**
- **current or past history of smoking, and a confirmed family history of BE or EAC (in a first-degree relative) (strong recommendation, moderate level of evidence.**
- **If endoscopy reveals esophagitis (Los Angeles Classification B, C, D), repeat endoscopic assessment after PPI therapy for 8–12 weeks is recommended to ensure healing of esophagitis and exclude the presence of underlying BE (conditional recommendation, low level of evidence).**

- **Patients with BE should receive once-daily PPI therapy. Routine use of twice-daily dosing is not recommended, unless necessitated because of poor control of reflux symptoms or esophagitis**
- **Endoscopic surveillance should employ four-quadrant biopsies at 2 cm intervals in patients without dysplasia and 1 cm intervals in patients with prior dysplasia.**
- **For BE patients without dysplasia, endoscopic surveillance should take place at intervals of 3 to 5 years (strong recommendation, moderate level of evidence).**
- **For patients with indefinite for dysplasia, a repeat endoscopy after optimization of acid suppressive medications for 3–6 months should be performed. If the indefinite for dysplasia reading is confirmed on this examination, a surveillance interval of 12 months is recommended (strong recommendation, low level of evidence).**
- **For patients with confirmed low-grade dysplasia and without life-limiting comorbidity, endoscopic therapy is considered as the preferred treatment modality, although endoscopic surveillance every 12 months is an acceptable alternative (strong recommendation, moderate level of evidence).**
- **Patients with BE and confirmed high-grade dysplasia should be managed with endoscopic therapy unless they have life-limiting comorbidity (strong recommendation, high level of evidence).**

Patients with nodularity in the BE segment should undergo endoscopic mucosal resection of the nodular lesion(s) as the initial diagnostic and therapeutic maneuver. Histologic assessment of the EMR specimen should guide further therapy. In subjects with EMR specimens demonstrating HGD, or IMC, endoscopic ablative therapy of the remaining BE should be performed (strong recommendation, high level of evidence).

- **In patients with EMR specimens demonstrating neoplasia at a deep margin, residual neoplasia should be assumed, and surgical, systemic, or additional endoscopic therapies should be considered (strong recommendation, low level of evidence).**
- **In patients with dysplastic BE who are to undergo endoscopic ablative therapy for nonnodular disease, radiofrequency ablation is currently the preferred endoscopic ablative therapy (strong recommendation, moderate level of evidence).**

Clinical Features

- **Progressive dysphagia**
- **Odynophagia**
- **Weight loss**
- **Nausea, vomiting, hematemesis**
- **Involvement of adjacent structures (chronic cough, hoarseness,)**
- **Metastasis (hepatomegaly, bony pains, left supraclavicular adenopathy)**

Investigations

- **Barium swallow**

  persistent filling defect, shouldering

  can't detect small lesions, sensitivity 75%
- **Endoscopy**

  brushing and biopsy for cytology

For staging

- **Endoscopic ultrasound**
- **C.T. scan**
- **Mediastinotomy or laparotomy**
- **PET scan**

TNM CLASSIFICATION FOR ***STAGING***		
T	**Tx:**	The primary tumor can’t be assessed.
	T0:	There is no evidence of a primary tumor.
	Tis:	The cancer is only in the epithelium (the top layer of cells lining the inside of the esophagus). It has not started growing into the deeper layers. This stage is also known as *high-grade dysplasia*.
	T1a:	The cancer is growing into the lamina propria or muscularis mucosa (the tissue under the epithelium).
	T1b:	The cancer has grown through the other layers and into the submucosa.
	T2:	The cancer is growing into the thick muscle layer (muscularis propria).
	T3:	The cancer is growing into the outer layer of the esophagus (the adventitia).
	T4a:	The cancer is growing into the pleura (the thin layer of tissue covering the lungs), the pericardium (the thin sac surrounding the heart), or the diaphragm (the muscle below the lungs that separates the chest from the abdomen).
	T4b:	The cancer has grown into the trachea (windpipe), the aorta (the large blood vessel coming from the heart), the spine, or other crucial structures.
N	**Nx:**	No description of lymph node involvement possible because of incomplete information.
	N0:	The cancer has not spread to nearby lymph nodes
	N1:	The cancer has spread to 1 or 2 nearby lymph nodes.
	N2:	The cancer has spread to 3 to 6 nearby lymph nodes.
	N3:	The cancer has spread to 7 or more nearby lymph nodes.
M	**M0:**	The cancer has not spread (metastasized) to distant organs or lymph nodes.
	M1:	The cancer has spread to distant lymph nodes and/or other organs. (Common sites of spread include the liver and lungs.)

Staging classification

Stage IA	**T1**	**N0**	**M0**
Stage IB	**T2**	**N0**	**M0**
Stage IIA	**T2,T3**	**N0**	**M0**
Stage IIB	**T1,T2**	**N1**	**M0**
	T2,T3	**N0**	**M0**
Stage IIIA	**T1,T2**	**N2**	**M0**
	T3	**N1**	**M0**
	T4a	**N0**	**M0**
Stage IIIB	**T3**	**N2**	**M0**
Stage IIIC	**T4a**	**N1,N2**	**M0**
	T4b	**Any N**	**M0**
	Any T	**N3**	**M0**
Stage IV	**Any T**	**Any N**	**M1**

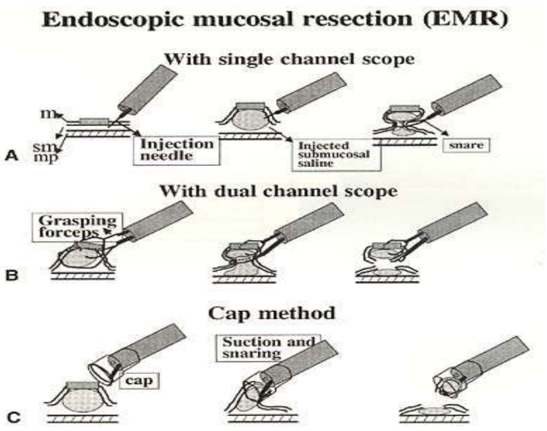
Treatment

Management

- **Treatment of esophageal cancer varies by disease stage, as follows:**
- **Stage I-III (locoregional disease) - Available modalities are endoscopic therapies (e.g., mucosal resection or ablation), esophagectomy, preoperative chemoradiation, and definitive chemoradiation.**
- **Stage IV – Systemic chemotherapy with palliative/supportive care**
- **Options include**

  1. *Endoscopic*
     - **endoscopic mucosal resection,**
     - **endoscopic submucosal dissection and/or ablation) is preferred for high-grade dysplasia (HGD) or T1a tumors ≤2 cm; ablation alone is a primary treatment option for patients with HGD**
  2. *Surgical*

     Indications :



- **Esophageal cancer in a patient who is a candidate for surgery (esophagectomy)**
- **High-grade dysplasia in a patient with Barrett esophagus that cannot be adequately treated endoscopically**

Contraindications for surgical treatment

- **Metastasis to N2 (celiac, cervical, supraclavicular) nodes or solid organs (e.g., liver, lungs)**
- **Invasion of adjacent structures (e.g., recurrent laryngeal nerve, tracheobronchial tree, aorta, pericardium)**
- **Severe associated comorbid conditions (e.g., cardiovascular disease, respiratory disease)**

3. Palliative

for patients who are not candidates for surgery are as follows:

- **Chemotherapy**
- **Radiotherapy**
- **Laser therapy**
- **Stents**

Cancer Stomach

Epidemiology

- second most common cause of cancer-related death in the world after cancer lung.
- Adenocarcinoma of the stomach is the second most common cancer worldwide
- affects slightly more men than women
- median age for gastric cancer in the United States is 70 years for males and 74 years for females
- Incidence high in developing countries and lowest in developed nations.
  - Frequency of different types of gastric neoplasms
- Commonest type of gastric cancer is adenocarcinoma (90%),
- followed by gastric lymphoma(5%),
- gastrointestinal stromal tumor (GIST 2%),
- carcinoid (1%)

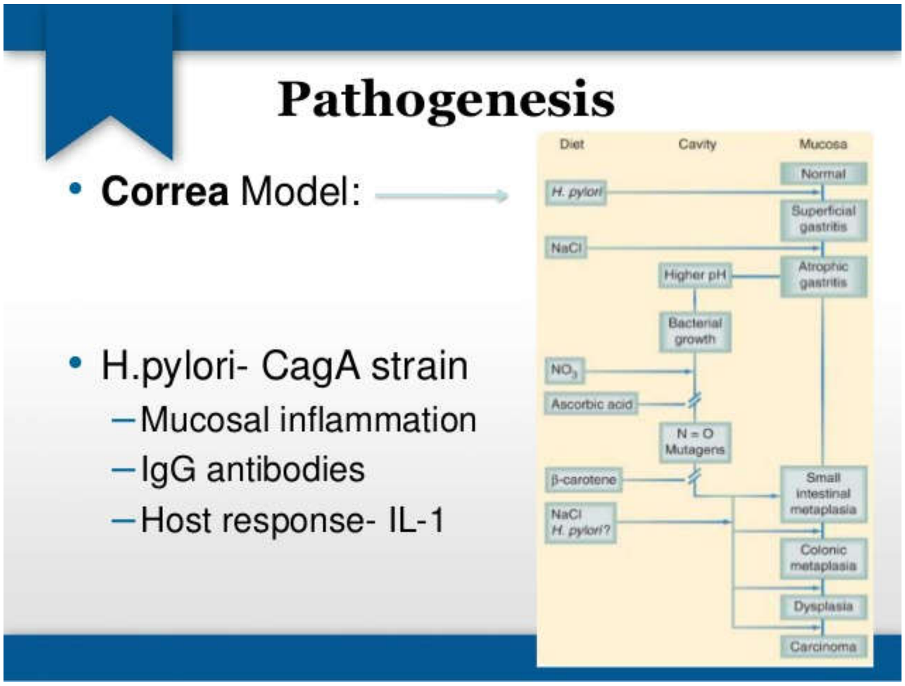
Pathogenesis

- No single cause but multiple risk factors
- Two separate forms:

- intestinal (well differentiated)
- diffuse (undifferentiated)

- A key difference is the presence or absence of intercellular adhesion molecule produced by the E- cadherin gene
- Familial gastric cancers
- Hereditary diffuse gastric cancer syndrome is caused by a germline mutation in *CDH1* (encoding cadherin 1) critical for establishing intercellular connections and maintaining organization of epithelial tissue
- The inheritance is autosomal dominant
- the risk of developing multifocal gastric adenocarcinoma (GAC) is up to 80% in mutation carriers.
- Currently, prophylactic gastrectomy is recommended in afflicted individuals once they are >20 years of age.

- The intestinal type is related to H pylori and tumor cells tend to occur in tubular or glandular formations
- Correa cascade



Pathogenesis

- **Correa** Model:
- H.pylori- CagA strain
  - Mucosal inflammation
  - IgG antibodies
  - Host response- IL-1

Risk factors

Several factors are implicated in the development of gastric cancer, including :

- Diet (nitrosocompounds, high salt, high in processed meat and low fuits particularly citrus)
- *Helicobacter pylori* infection,
- Smoking
- Pernicious anemia,
- Adenomatous polyps,
- Chronic atrophic gastritis,
- Prior radiation exposure or inherited syndromes.

Symptoms

- **Might be vague**
- **Weight loss and mid epigastric pain**
- **Dyspepsia , nausea or early satiety,**
- **dysphagia**
- **postprandial fullness, loss of appetite,**
- **melena, hematemesis,**
- **Paraneoplastic as (Leser Trelat, venous thrombosis, and dermatomyositis)**

Signs

All physical signs are late events and include:

- **succession splash; hepatomegaly;**
- **periumbilical metastasis (Sister Mary Joseph nodule);**
- **enlarged lymph nodes : Virchow nodes (i.e., left supraclavicular) and Irish node (anterior axillary).**
- **Blumer shelf (i.e., shelf like tumor of the anterior rectal wall) may also be present.**

Laboratory studies

- **CBC: anemia due to bleeding, liver dysfunction, or poor nutrition. (30% of patients).**
- **Electrolyte panels**
- **Liver function tests.**
- **Carcinoembryonic antigen (CEA) is increased in 45-50% of cases.**
- **Cancer antigen (CA) 19-9 is elevated in about 20% of cases**

Imaging

Endoscopy

- **Permits tissue diagnosis of suspected lesions.**
- **Biopsy of any ulcerated lesion should require at least 6 biopsies taken from around the lesion because of variable malignant transformation**
- **Appears as exophytic polypoid mass**

- **Proximal lesions are more aggressive with worse prognosis and distal lesions are related to H pylori**

For *staging* of the tumor

- **CT of chest and abdomen**
- **Endoscopic ultrasound with FNA of suspected nodes helpful in assessing depth of penetration of the tumor or involvement of adjacent structures**
- **PET scan**

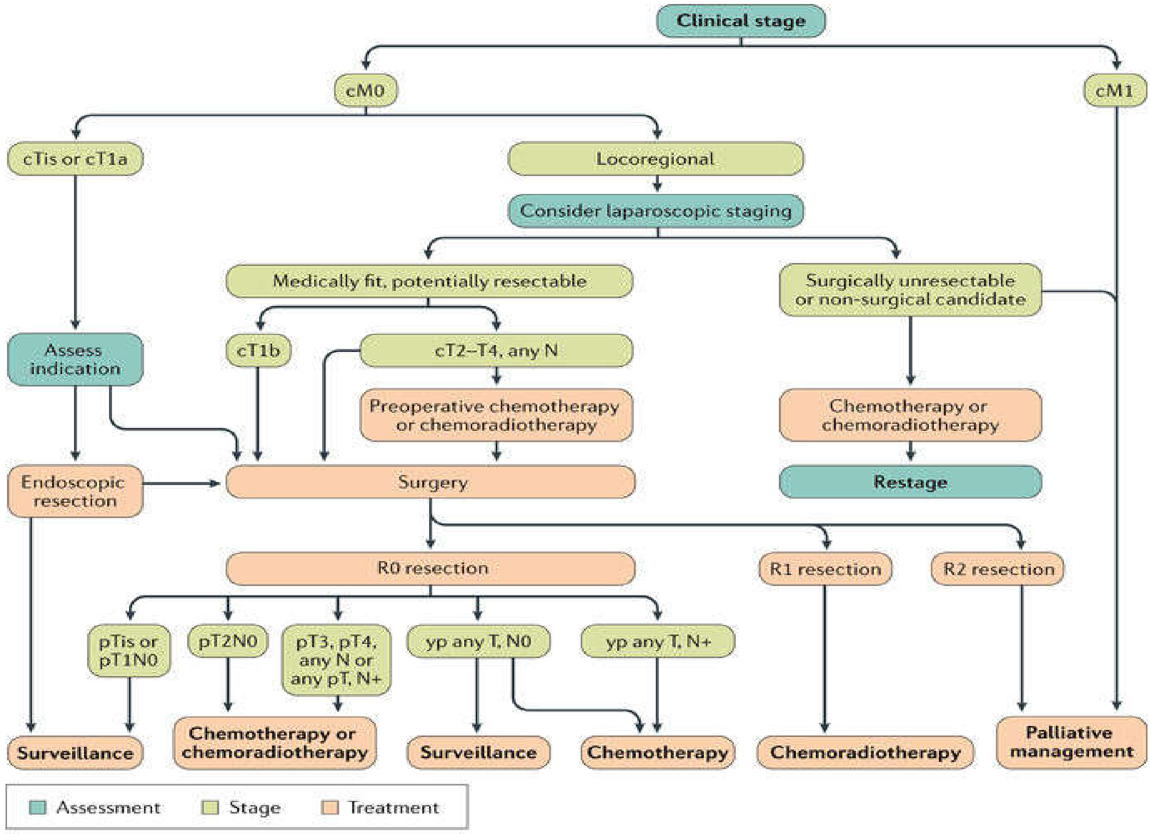
TNM classification system for staging gastric carcinoma		
Primary tumor	TX -	Primary tumor (T) cannot be assessed
	T0 -	No evidence of primary tumor
	Tis -	Carcinoma in situ, intraepithelial tumor without invasion of lamina propria
	T1 -	Tumor invades ***lamina propria*** or ***submucosa***
	T2 -	Tumor invades ***muscularis propria*** or ***sub-serosa***
	T3 -	Tumor penetrates ***serosa*** (i.e., visceral peritoneum) *without* invasion of adjacent structures
	T4 -	Tumor invades ***adjacent structures***
Regional lymph nodes	**NX**	- Regional lymph nodes (N) cannot be assessed
	N0	- No regional lymph node metastases
	N1	- Metastasis in 1-6 regional lymph nodes
	N2	- Metastasis in 7-15 regional lymph nodes
	N3	- Metastasis in more than 15 regional lymph nodes
Distant metastasis	**MX**	- Distant metastasis (M) cannot be assessed
	M0	- No distant metastasis
	M1	- Distant metastasis

Stage	**T**	**N**	**M**
٠	**Tis**	**N0**	**M0**
IA	**T1**	**N0**	**M0**
IB	**T2**	**N0**	**M0**
	T1	**N1**	**M0**
IIA	**T3**	**N0**	**M0**
	T2	**N1**	**M0**
	T1	**N2**	**M0**
IIB	**T4a**	**N0**	**M0**
	T3	**N1**	**M0**
	T2	**N2**	**M0**
	T1	**N3**	**M0**
IIIA	**T4a**	**N1**	**M0**
	T3	**N2**	**M0**
	T2	**N3**	**M0**
IIIB	**T4b**	**N0**	**M0**
	T4b	**N1**	**M0**
	T4a	**N2**	**M0**
	T3	**N3**	**M0**
IIIC	**T4b**	**N2**	**M0**
	T4b	**N3**	**M0**
	T4a	**N3**	**M0**
IV	**Any T**	**Any N**	**M1**

Treatment

- **Resectable →surgery + adjuvant chemoradiotherapy**
- **Advanced → palliative measures**

1. **Chemotherapy**
2. **Radiotherapy**
3. **Palliative surgical procedures as gastrojejunostomy or endoscopic stent**



Nature Reviews | Disease Primers

Gastric lymphoma

- **Accounts for 20% of all extra nodal lymphoma**
- **Peak incidence between 50 and 60 years**
- **Risk factors include Hpylori infection, autoimmune disease , long term immunosuppressive and celiac disease**

Clinical features

Abdominal discomfort, anorexia, early satiety, wt loss, gastric outlet obstruction , may be fever and night sweat.

Diagnosis

Endoscopically, large firm rugal folds, eroded nodules, polypoid mass

- 2 histologic subtypes
- Extranodal marginal zone B-cell lymphoma(MALT lymphoma), low grade neoplasm, specific type of nonHodgkin lymphoma, related to Hpylori
- Diffuse large B-cell lymphoma
- Heterogenous group of nonHodgkin lymphoma, either occur de novo or transformation from MALT lymphoma

Staging

- **Stage I: confined to stomach**
- **Stage II: involves lymph nodes within the abdomen**
- **Stage III: involvement on both sides of the diaphragm**
- **Stage IV: disseminated**

Treatment

- **Antimicrobial therapy alone if flat mucosal lesions in the stomach without lymph node involvement**
- **Otherwise systemic chemotherapy, radiotherapy or surgery**

Gastrointestinal *stromal* tumor

- (GISTs) account for less than 1% of gastrointestinal (GI) tumors,
- most common mesenchymal neoplasms of the gastrointestinal tract.
- in 1998, the actual cell of origin of GISTs is a pluripotential mesenchymal stem cell programmed to differentiate into the interstitial cell of Cajal
- express *KIT* and are developmentally dependent on stem cell factor, which is regulated through *KIT* kinase. Perhaps the most critical development that distinguished GISTs as a unique clinical entity was the discovery of c-*kit* proto-oncogene mutations in these tumors.
- submucosal lesions, which most frequently grow endophytically in parallel with the lumen of the affected structure. GISTs may also manifest as exophytic extraluminal excrescences.
- range in size from smaller than 1 cm to as large as 40 cm in diameter. [15]
- Approximately 50-70% of GISTs originate in the stomach, 20-30% of GISTs arising from the jejunoileal. Less frequent sites of occurrence include the colon and rectum (5-15%) and esophagus (<5%).

Clinical picture

The most common symptoms are

- vague, nonspecific abdominal pain or discomfort, early satiety and rarely an abdominal mass is palpable.
- symptoms secondary to obstruction or hemorrhage..
- manifestations of anemia as malaise, fatigue, or exertional dyspnea with significant blood loss.

Diagnosis

Barium swallow	EUS	Endoscopy	PET for staging
u/s	C.T. abdomen	MRI abdomen	

Histological findings

- (GISTs) manifest a wide variety of clinical behavior, from slow-growing indolent tumors to aggressive malignant cancers with the propensity to invade the adjacent organs,
- GISTs typically stain intensely for the CD117 molecule, which is an epitope of KIT.

Treatment

Imatinib is a selective small molecule inhibitor of a family of structurally similar tyrosine kinase signaling enzymes, including KIT

- inhibit the proliferation (GIST) cells with *KIT* mutations.
- indicated in patients with advanced GISTs.
- adjuvant therapy after complete surgical resection in patients with tumors that are stratified to be high risk
- and as neoadjuvant therapy, with the goal of tumor shrinkage prior to surgical resection

Prognosis

The prognostic factors include:

- the size of the tumor,
- location of the tumor (gastric better than other sites)
- and the mitotic rate(mitotic rate of 10 or greater per 50 high-power fields (HPFs) had a median survival rate of 18 months, compared with an 80%, 8-year disease-free survival rate in patients who had curative resections and tumors with a mitotic rate less than 10/50 HPFs
- the ability or inability to achieve completely negative resection margins.

Colorectal Cancer

0 **Disease of urban society**

0 **Incidence decreasing gradually due to screening programs.**

Types:

- ***Primary***: 95% ***adeno*-carcinoma**

5% lymphoma, carcinoid, leiomyosarcoma

- ***Metastatic*** lesions to colorectum: lymphoma, malignant melanoma, leiomyosarcoma, adenocarcinoma of breast, ovaries, prostate.

Incidence and epidemiology

Second leading cause of **death** from cancer in U.S.

Incidence

0 highest in U.S., east and west Europe, Japan,

0 lowest in Africa and Asia

Etiology and pathogenesis

- Host and ***environmental*** *factors*	***- Inflammatory bowel disease***
=Age: (95% >**45** years) =Personal and family **history** of colorectal neoplasia =Familial adenomatous polyposis (**FAP**) =Dietary components: (excess red meat, high fat, low vegetables and fruits =**obesity**	in **U.C.** extent and duration in **Crohn's** duration of disease
- Others type 2 DM, acromegaly, pelvic irradiation, utero-sigmoido-stomy	- ***Lifestyle*** alcohol, tobacco risk physical activity risk
- Genetic factors CCC develops due to genetic mutations in loci involved in control of cell growth. progression from normal colonocytes to adenotamous tissue involves stepwise accumulation of mutations, each of which provides a growth advantage to affected cells	

pathways for colorectal cancer

chromosomal instability (conventional pathway)

- uneven distribution of genetic material in daughter cells leads to aneuploidy.

microsatellite instablity

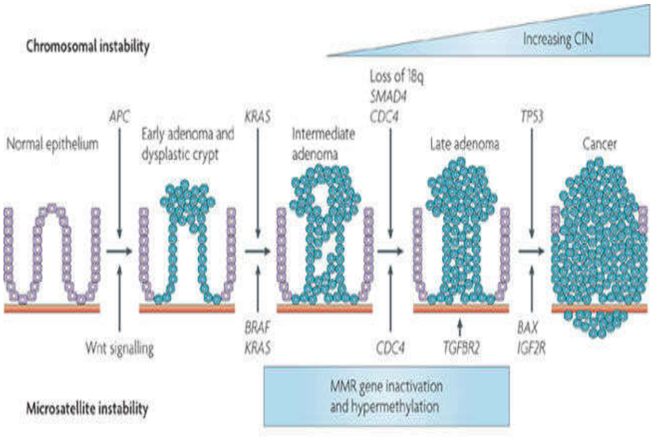
- loss of mismatch repair activity
- leads to miocrosateelite unstable tumors

Serrated pathway

- Progress from serrated polyp

Chromosomal instability

- **Initial event is somatic mutation in APC gene (gene that regulates cell death) increased proliferation of affected cells and adenoma formation.**
- **Subsequent mutation in K-ras cellular proto-oncogene leads to further growth dysregulations.**
- **Mutations of P53tumor suppresion gene transition from adenoma to carcinoma**
- **Replication of these defective cells leads to loss of chromosomal segments containing several alleles→ loss of heterozygosity deletion of other tumor suppression genes as DCC.**
- **Eventually the cell acquire the capability to invade and metastasize, at which point the tumor is considered malignant.**

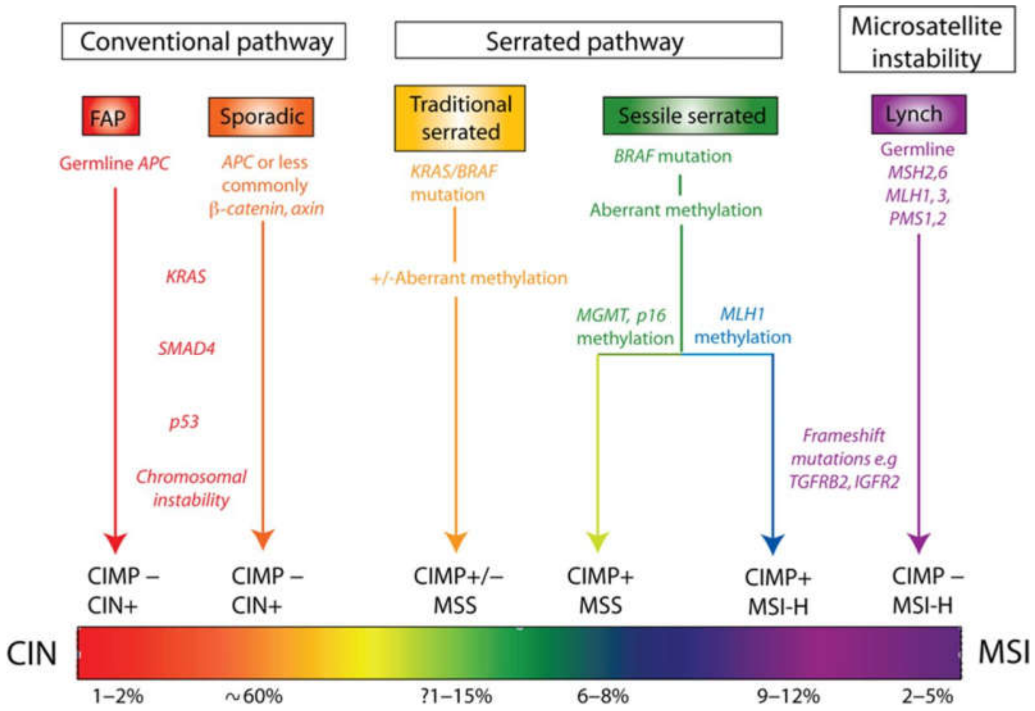


Nature Reviews | Cancer

Microsatellite instability and HNPCC

- **HNPCC is an autosomal dominant disease characterized by occurrence within a family, of multiple cases of colorectal cancer in the absence of polyposis.**
- **Due to mutation in mismatch repair genes (hMSH2, hMLH1m, hPMS1, hPMS2, hMSH6)which normally corrects errors in DNA replication cancer formation.**
- **HNPCC (Lynch syndrome) is distinguished from sporadic colorectal cancer**
- **(mean age 40),**

- **higher risk of synchronous tumors (18% versus 6%), right sided tumors (60% versus 20%),**
- **more frequent mucinous tumors.**



Clinical features

- **Age > 59**
- **Symptoms related to tumor size and location:**

Proximal (caecum to splenic flexure)	***Distal*** tumors (descending colon and rectum)
ill-defined abdominal pain weight loss occult bleeding	altered bowel habits decrease stool calibre hematochezia late intestinal obstruction

Investigations

Lab studies

CBC: nomal or iron deficiency anemia

LFT: if high suspect liver metastasis

CEA: increased in most but not all cases

Endoscopic studies

colonoscopy is the procedure of choice

visualize, take biopsy, polypectomy

sensitivity 100% in lesions > 1 cm

Radiographic studies

- Double contrast barium enema

technical limitations in assessing rectosigmoid (+ flexible sigmoidoscopy)

misinterpretation in inexperienced hands)

- abdominal C.T. and chest X ray to exclude metastasis

Staging

***Dukes* classification:**

CIS	malignant lesions that do not penetrate muscularis mucosa cured by adequate endoscopic or surgical resection		
Dukes stage **A**	invasive cancer confined to submucosa		
Dukes stage **B**	**B1**	invading muscularis propria	
	B2	extending to the serosa	
Dukes stage **C**	**C1**	**(1 – 4 nodes)**	***regional*** lymph node involvement
	C2	**(> 4 nodes)**	
Dukes stage D	distant metastasis		

= = Other classifications include TNM classification and Astler - coller systems.

Prognosis

estimated by the tumor stage

according to Dukes classification

age adjusted 5 year survival is:

Dukes stage A	**95 – 100%**
Dukes stage B	**80 – 85%**
Dukes stage C	**50 – 70%**
Dukes stage D	**5 – 15%**

Treatment

Resectable	**Unresectable**
(surgery and adjuvent therapy) - right hemicolectomy (cecum, ascending, transverse) - Left hemicolectomy (splenic flexure, descending) - Sigmoid colectomy - Total abdominal colectomy with ileoanal anastomosis	- Palliative - ND:YAG laser photocoagulation - Endoscopic placement of self-expanding metal endoluminal stent

Screening

Guidelines on colorectal screening have been issued by the following organizations:

- American Cancer Society (ACS), US Multi-Society Task Force on Colorectal Cancer, and American College of Radiology
- U.S. Preventive Services Task Force (USPSTF)
- American College of Physicians (ACP)
- American College of Gastroenterology (ACG)
- National Comprehensive Cancer Network (NCCN)
- In June 2017 the US Multi-Society Task Force on Colorectal Cancer issued updated screening recommendations that divide screening tests into three tiers, based upon their effectiveness.

Tier 1 tests consist of the following:

- Colonoscopy every 10 years
- Annual FIT

Tier 2 tests consist of the following:

- CT colonography every 5 years
- FIT–fecal DNA every 3 years
- Flexible sigmoidoscopy every 5–10 years
- **Tier 3 testing is capsule colonoscopy every 5 years**

*Suggested timing of **initial** screening and intervals for subsequent testing for different risk populations are as follows:*

- **For patients at average risk, testing with a tier 1 test should begin at age 45 years for African Americans and at age 50 for patients of all other races.**
- **For patients with a family history of colorectal cancer or advanced adenoma that was diagnosed before age 60 years in one first-degree relative or at any age in two first-degree relatives, testing should begin with colonoscopy at an age10 years younger than the youngest age at diagnosis of a first-degree relative, or age 40, to be repeated every 5 years.**
- **In patients with one first-degree relative with colorectal cancer, advanced adenoma, or an advanced serrated lesion diagnosed at age 60 or older, screening should begin with a tier 1 test at age 40 and continue at the same intervals as in average-risk patients.**
- **Colonoscopy screening should be discontinued in patients aged 75 or older with prior negative screening tests or whose life expectancy is less than 10 years, or in those 85 years or older without prior screening.**

Cancer *pancreas*

- **malignant neoplasm of the pancreas**
- **Endocrine or exocrine**
- **95% of exocrine pancreatic cancers are adeno-carcinomas .**
- **5% include adeno-squamous carcinomas, signet ring cell carcinomas, hepatoid carcinomas, colloid carcinomas, undifferentiated carcinomas, and undifferentiated carcinomas with osteoclast-like giant cells**

Presentation

- **early does not cause symptoms,**
- **later symptoms are usually non-specific and varied.**
- **often not diagnosed until it is advanced.**
- **Common symptoms include:**

-*Pain in upper abdomen* that typically radiates to the back (seen in carcinoma of the body or tail of the pancreas)

-*Loss of appetite* and/or nausea and vomiting

- **Significant weight loss**

- Painless jaundice (yellow skin/eyes, dark urine)
- steatorrhea
- Trousseau sign
- Diabetes mellitus.
- Clinical depression has been reported in association with pancreatic cancer

Predisposing factors

- Age (particularly over 60)
- Male gender
- African-American ethnicity
- Smoking .
- Diets (low in vegetables and fruits, high in red meat)
- obesity
- Diabetes mellitus is both risk factor for pancreatic cancer, and, as noted earlier, new onset diabetes can be an early sign of the disease

- Chronic pancreatitis has been linked, but is not known to be causal. The risk of pancreatic cancer in individuals with familial pancreatitis is particularly high.
- Family history, 5–10% of pancreatic cancer patients have a family history of pancreatic cancer.

Signs

- pancreatitis are sometimes noted.
- Courvoisier sign defines the presence of jaundice and a painlessly distended gallbladder as strongly indicative of pancreatic cancer, and may be used to distinguish pancreatic cancer from gallstones.
- Tiredness, irritability and difficulty eating due to pain also exist. Pancreatic cancer is usually discovered during the course of the evaluation of aforementioned symptoms.

Lab investigations

- Liver function tests

results indicative of bile duct obstruction (raised conjugated bilirubin, γ-glutamyl transpeptidase and alkaline phosphatase levels).

- CA19-9

frequently elevated in pancreatic cancer.

lacks sensitivity and specificity. When a cutoff above 37 U/mL is used, this marker has a sensitivity of 77% and specificity of 87% in discerning benign from malignant disease. CA 19-9 might be normal early in the course, and could be elevated due to benign causes of biliary obstruction.

Imaging

- *CT scan*

can be used to identify the location of the cancer.

- *Endoscopic ultrasound* (EUS)

visualize the location

serve to guide a percutaneous needle biopsy, which is necessary to establish a definitive diagnosis.

- *PET SCAN*

Staging

Stage **0**	carcinoma **in situ**	abnormal cells in lining of pancreas
Stage **I**	cancer has formed and is found in pancreas only	stage IA: tumor 2cms or less stage IB: tumor> 2 cms
Stage **II**	*Stage II **A***:	cancer has spread to nearby tissue and organs but not to nearby lymph nodes
	*Stage II **B***:	cancer has spread to nearby lymph nodes and may have spread to nearby tissues and organs
Stage **III**	Cancer has spread to the major blood vessel near the pancreas and may have spread to nearby lymph nodes.	
Stage **IV**	Cancer may be of any size and has spread to distant organs, such as liver, lung, and peritoneal cavity.	

Treatment

- If **operable**; ***Surgery***
- Treatment depends on the stage and site of the cancer.
- **Whipple** operation; for cancers involving the head of the pancreas.
- can only be performed if the patient is likely to survive major surgery, if the cancer is localized without invading local structures or metastasizing
- can therefore only be performed in the minority of cases.
- Distal pancreatectomy for cancers in tail of pancreas.
- spleen-preserving distal pancreatectomy can also be used as a method to remove a cancer running through centre of pancreas; this is invasive surgery, resulting in loss of body and tail.

Adjuvant therapy

- Postoperative *adjuvant* ***chemo*****-**therapy with ***gemcitabine*** has been shown to significantly increase the 5-year survival (from approximately 10 to 20%), and should be offered if the patient is fit after surgery
- Addition of ***radio*****-**therapy is a hotly debated topic.

Palliative Treatment

***Chem**otherapy:*

Gemcitabine,5-flurouracil, cisplatin

Chemo-radiation:

Conformal radiotherapy+ 5-flurouracil

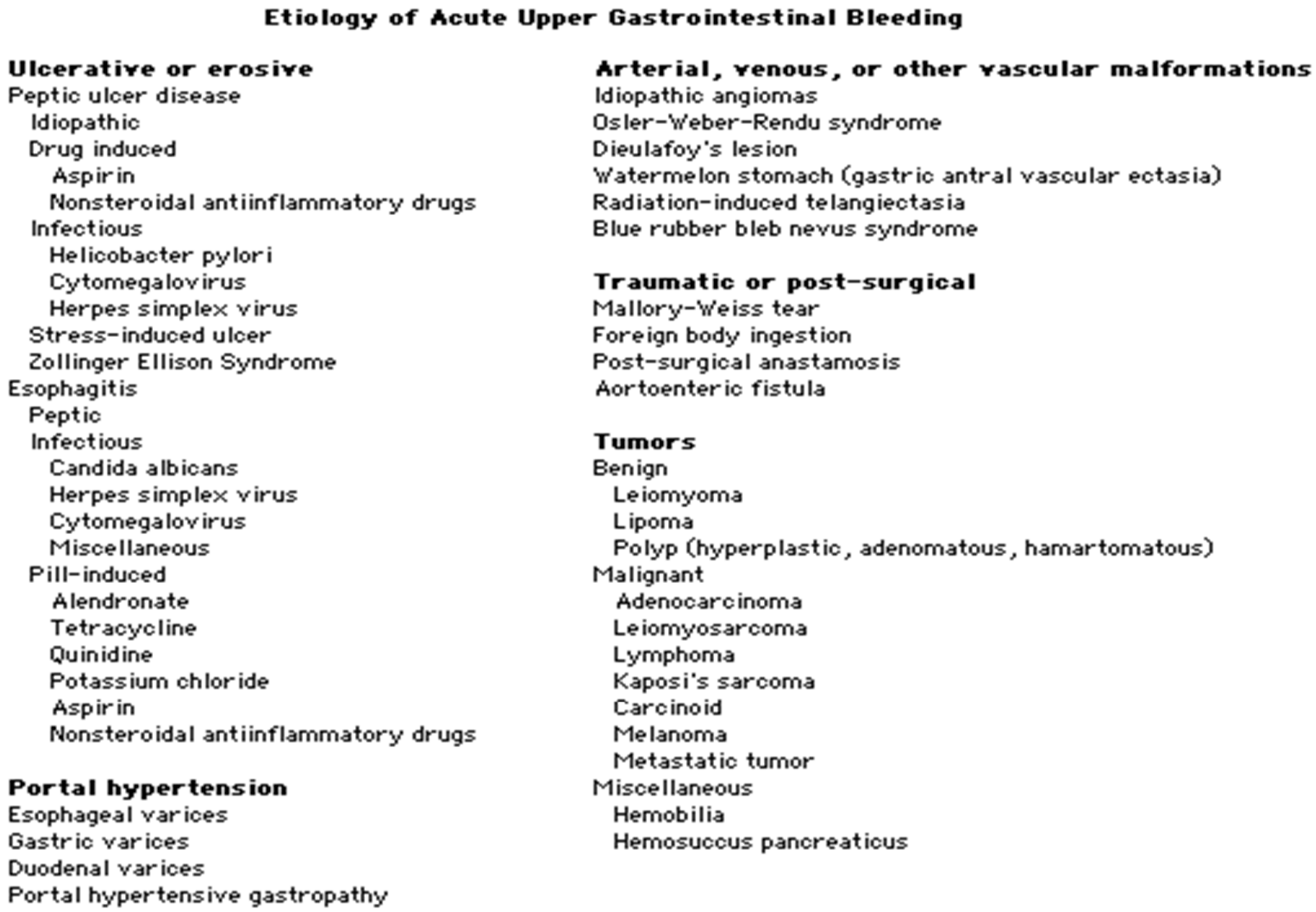
- *Palliative* **Surgery** can be performed for palliation, if the malignancy is invading or compressing the CBD, *duodenum* or colon.

- **Endoscopic placement** of *self-expandable metallic* ***stent*** in *CBD* (obstructive jaundice), or in the *duodenum* (duodenal invasion) is an alternative in selected cases

Gastrointestinal Bleeding

Types of GI Bleeding

- Upper
- Lower
- Occult
- Obscure



Etiology of Acute Upper Gastrointestinal Bleeding

Ulcerative or erosive

- Peptic ulcer disease
  - Idiopathic
  - Drug induced
    - Aspirin
    - Nonsteroidal antiinflammatory drugs
  - Infectious
    - Helicobacter pylori
    - Cytomegalovirus
    - Herpes simplex virus
  - Stress-induced ulcer
  - Zollinger Ellison Syndrome
- Esophagitis
  - Peptic
  - Infectious
    - Candida albicans
    - Herpes simplex virus
    - Cytomegalovirus
    - Miscellaneous
  - Pill-induced
    - Alendronate
    - Tetracycline
    - Quinidine
    - Potassium chloride
    - Aspirin
    - Nonsteroidal antiinflammatory drugs

Portal hypertension

- Esophageal varices
- Gastric varices
- Duodenal varices
- Portal hypertensive gastropathy

Arterial, venous, or other vascular malformations

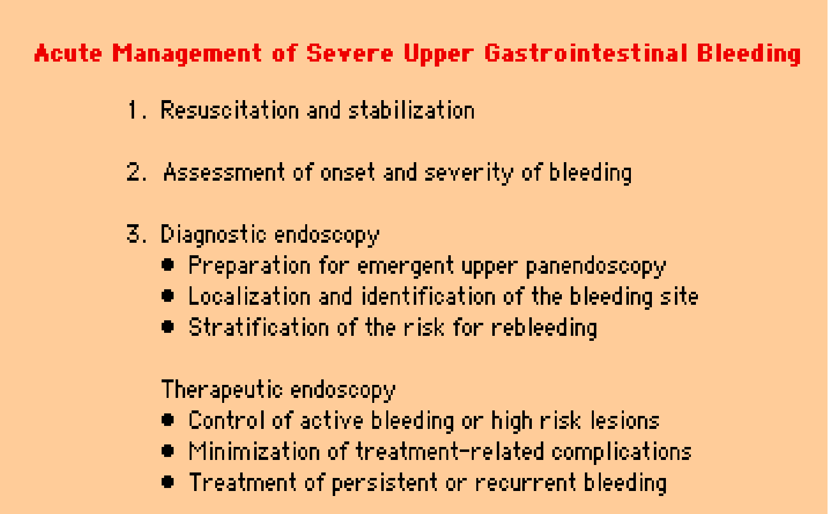
- Idiopathic angiomas
- Osler-Weber-Rendu syndrome
- Dieulafoy's lesion
- Watermelon stomach (gastric antral vascular ectasia)
- Radiation-induced telangiectasia
- Blue rubber bleb nevus syndrome

Traumatic or post-surgical

- Mallory-Weiss tear
- Foreign body ingestion
- Post-surgical anastamosis
- Aortoenteric fistula

Tumors

- Benign
  - Leiomyoma
  - Lipoma
  - Polyp (hyperplastic, adenomatous, hamartomatous)
- Malignant
  - Adenocarcinoma
  - Leiomyosarcoma
  - Lymphoma
  - Kaposi's sarcoma
  - Carcinoid
  - Melanoma
  - Metastatic tumor
- Miscellaneous
  - Hemobilia
  - Hemosuccus pancreaticus



Acute Management of Severe Upper Gastrointestinal Bleeding

1. Resuscitation and stabilization

2. Assessment of onset and severity of bleeding

3. Diagnostic endoscopy
   - Preparation for emergent upper panendoscopy
   - Localization and identification of the bleeding site
   - Stratification of the risk for rebleeding

   Therapeutic endoscopy
   - Control of active bleeding or high risk lesions
   - Minimization of treatment-related complications
   - Treatment of persistent or recurrent bleeding

PH - UGI Bleeding

Endoscopy in PH

- *Diagnosis*
  - Presence
  - Assessment of severity
  - Prediction of bleeding
  - *"Primary Prophylaxis"*
  - PHG
- *Therapeutic*
  - Treatment of bleeding
  - Prevention of recurrent Bleeding *"secondary prophylaxis"*
  - Follow Up
  - PHG

Diagnostic endoscopy

Predictors of Progression of Cirrhosis

- Alcoholic

- Child B or C

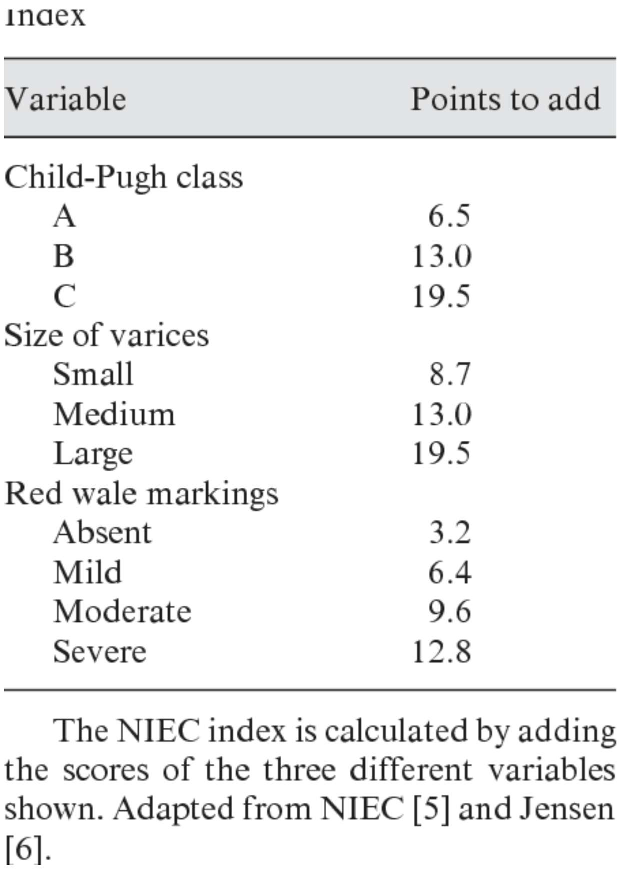
- Red Wale signs

☐ **Variceal Size > 5 mm = predictor of bleeding**

Endoscopic Classification of Esophageal Varices

- **Paquet system attempts to identify pts who are likely to bleed from varices to be candidates for prophylactic EST**
-
- **Paquet's classification four grades.**

=The North Italian Endoscopy Club (NIEC) Index


index

Variable	Points to add
Child-Pugh class	
A	6.5
B	13.0
C	19.5
Size of varices	
Small	8.7
Medium	13.0
Large	19.5
Red wale markings	
Absent	3.2
Mild	6.4
Moderate	9.6
Severe	12.8

The NIEC index is calculated by adding the scores of the three different variables shown. Adapted from NIEC [5] and Jensen [6].

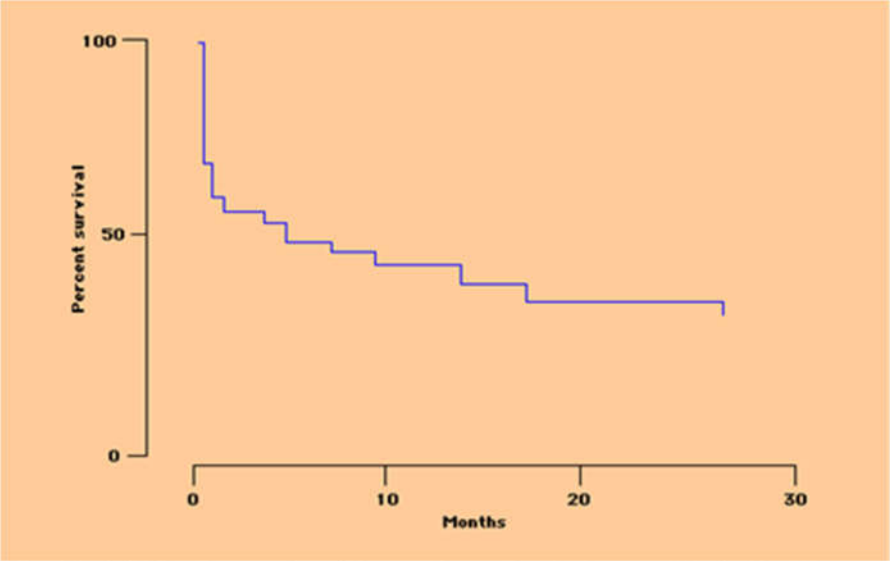
= Like hood of variceal bleeding according to NIEC Index

Score	*Rate of bleeding (%)*
< 20	**7**
20-30	**16-26**
30-40	**28-59**
> 40	**69**

Primary Prophylaxis

- **B- blocker therapy = Standard**
- **Hemodynamic responders = HVPG < 12 or 20 % less than original**
- **Rebleeding**
  - **Responders = 10 %**
  - **Non responders = 64 %**
- **Survival**
  - **Responders = 95 %**
  - **Non responders = 52 %**
- **Prophylactic EST = *Inappropriate* option**
- **Prophylactic EVL = A potentially attractive**
  - **Equally effective to B-blocker**
  - **Indicated in :**
    - **Sensitive to B-blocker**

- **Contraindication to B-blocker**
- **Hemodynamic "Non responders"**



Survival following variceal hemorrhage Survival curve illustrating the poor prognosis after a first variceal bleed. Thirty percent die during the acute episode and only 30 to 40 percent are alive at two years. (Data from Graham, DY, Smith, JL, Gastroenterology 1981; 80:800.)

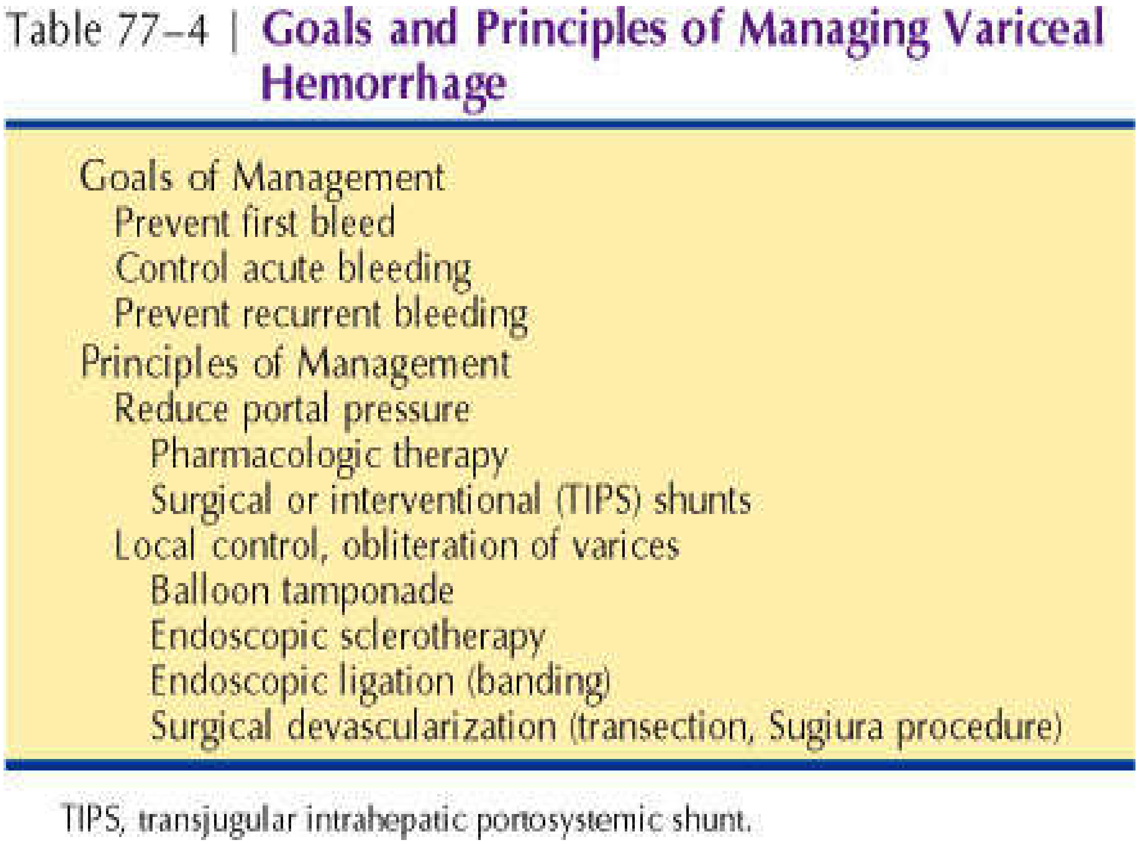


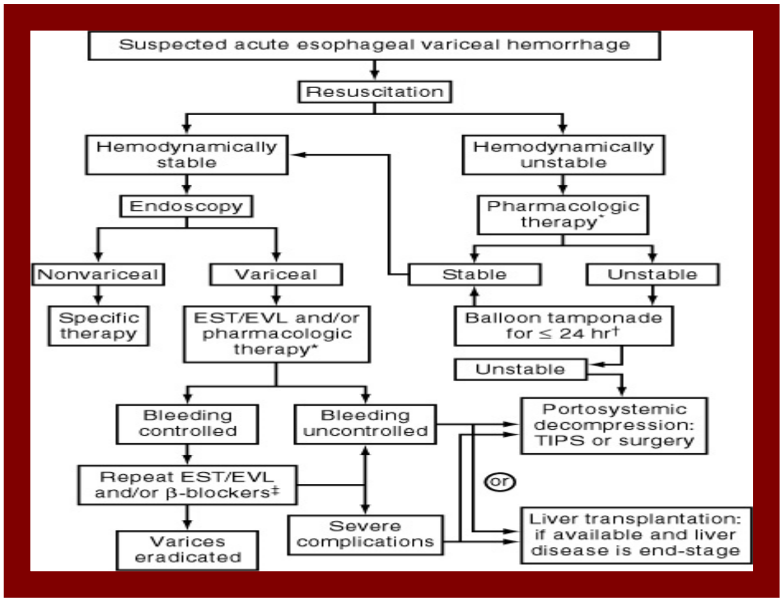
Table 77–4 | **Goals and Principles of Managing Variceal Hemorrhage**

- Goals of Management
  - Prevent first bleed
  - Control acute bleeding
  - Prevent recurrent bleeding
- Principles of Management
  - Reduce portal pressure
    - Pharmacologic therapy
    - Surgical or interventional (TIPS) shunts
  - Local control, obliteration of varices
    - Balloon tamponade
    - Endoscopic sclerotherapy
    - Endoscopic ligation (banding)
    - Surgical devascularization (transection, Sugiura procedure)

TIPS, transjugular intrahepatic portosystemic shunt.

Severity of Bleeding & *Re*-bleeding

- ☐ Mild
  - < 1g /dl
  - Minimal or no anemia
  - Stable hemodynamics
  - Infrequent melena
  - Coffee ground hematemesis
- ☐ Moderate
  - 1-2 g /dl
  - Anemia > 10 g/dl
  - Stable hemodynamics
  - Melena
  - Hematemesis
- ☐ Severe
  - > 2 g/dl drop
  - Anemia < 10 g /dl
  - Hemodynamic instability
  - Repeated hematemesis
  - Hematochezia or large vol. (> 350 ml)
- ☐ Rebleeding
  - > 1.5 g/dl
  - Recurrent hematemesis
  - Rec. or increased frequency melena or hematochezia


Suspected acute esophageal variceal hemorrhage
Resuscitation
Hemodynamically stable
Hemodynamically unstable
Endoscopy
Pharmacologic therapy*
Nonvariceal
Variceal
Stable
Unstable
Specific therapy
EST/EVL and/or pharmacologic therapy*
Balloon tamponade for ≤ 24 hr†
Unstable
Bleeding controlled
Bleeding uncontrolled
Portosystemic decompression: TIPS or surgery
Repeat EST/EVL and/or β-blockers‡
or
Varices eradicated
Severe complications
Liver transplantation: if available and liver disease is end-stage

Management of Bleeding P.H

- **Pharmacologic Therapy**
  - **Somatostatin**
  - **Octreotide**
  - **Terlipressin**
- **Balloon Tamponade (Sugestaken tube)**
- **Endoscopic**
- **TIPS**
- **Surgery**

Endoscopic Therapy

- **Endoscopy cornerstone manag. of GI Bleeding**
  - **Diagnostic**
  - **Therapeutic**
- **Rates of success & complications**
  - **Experience of the operator**
  - **Technique employed.**

Therapeutic Endoscopy in P.H

- **Esophageal Varices**
- **Gastric Varices**
  - **GOV1**
  - **GOV2**
  - **IGV1**
  - **IGV2**
  - **Other Varices**
  - **Duodenal**
  - **Rectal**

    - **PHG**

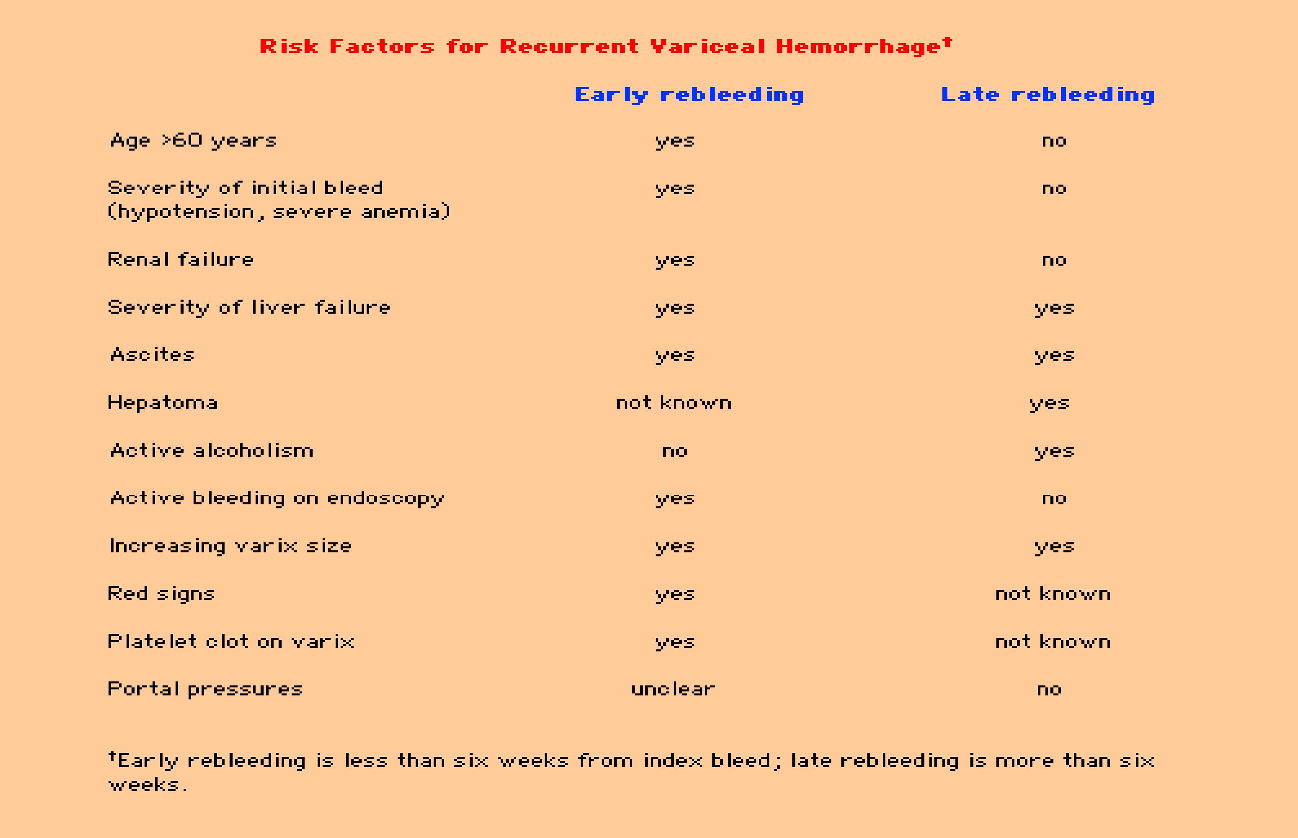
- **Sclerotherapy**
- **Multi-Band Ligation**
- **Tissue Adhesive**
- **Other**
    - **Tissue Adhesives**
    - **Other**
    - **Tissue Adhesives**
    - **APC**

Sclerotherapy in Acute bleeding

- **EST *treatment of choice* for active variceal hges.**
- **EST achieve control in 60% - 100% (90%).**
- **Major drawback of EST = complications.**

Complications of Sclerotherqpy

Minor	**Serious (Uncommon)**
Chest pain Temp. dysphagia, Fever Pleural effusions Strictures	Bacterial peritonitis Perforation Mediastinitis Brain abscess Spinal cord paralysis Pericarditis Portal vein thrombosis Aspiration pneumonia
Complications Related to Technique	**-Volume of sclerosant at injection site** **-Advanced liver disease pts prone to severe ulcers.** **=Control of bleeding is usually difficult** **=Severe coagulopathy results in oozing after injections.**



Risk Factors for Recurrent Variceal Hemorrhage[†]

	Early rebleeding	Late rebleeding
Age >60 years	yes	no
Severity of initial bleed (hypotension, severe anemia)	yes	no
Renal failure	yes	no
Severity of liver failure	yes	yes
Ascites	yes	yes
Hepatoma	not known	yes
Active alcoholism	no	yes
Active bleeding on endoscopy	yes	no
Increasing varix size	yes	yes
Red signs	yes	not known
Platelet clot on varix	yes	not known
Portal pressures	unclear	no

[†] Early rebleeding is less than six weeks from index bleed; late rebleeding is more than six weeks.

Why to continue Endoscopic Therapy after cessation of the First episode of bleeding “Prevention of Recurrent bleeding”

☐ **Expectant management alone, the risk of recurrent variceal bleeding is 47% - 84%.**

- **Schedule of Injections**

☐ **After control of bleeding, a follow-up session 2-3 days later is a common practice, usually followed by weekly or biweekly procedures until variceal obliteration.**

☐ **Surveillance for reappearance of varices is usually conducted at intervals that extend from 1 - 3 months & 6 monthly.**

- **Endpoints of Therapy**

☐ **Obliteration of varices**

☐ **Recurrence of varices and bleeding risk were significantly reduced if the varices were either**

  - **Obliterated or**
  - **Persisted as small white columns.**

☐ **Persistent small bluish varices were associated w continued risk of bleeding.**

Failure of Sclerotherapy

Definite	**Indefinite**
Inability to control acute bleeding from varices	Inability to obliterate varices
Recurrent bleeding after variceal obliteration	Nonfatal complications of the treatment
Death related to bleeding or Rx complications.	Recurrent bleeding prior to obliteration

Two bleeding episodes* while a pt is undergoing EST by an *experienced endoscopist

Factors Predict Failure of Sclerotherapy

10-30%

- ○ **Gastric fundal varices**
- ○ **Other varices**

(colon, duodenum, and unusual locations)

- ○ **PHG**

15- 20 % Causes not known

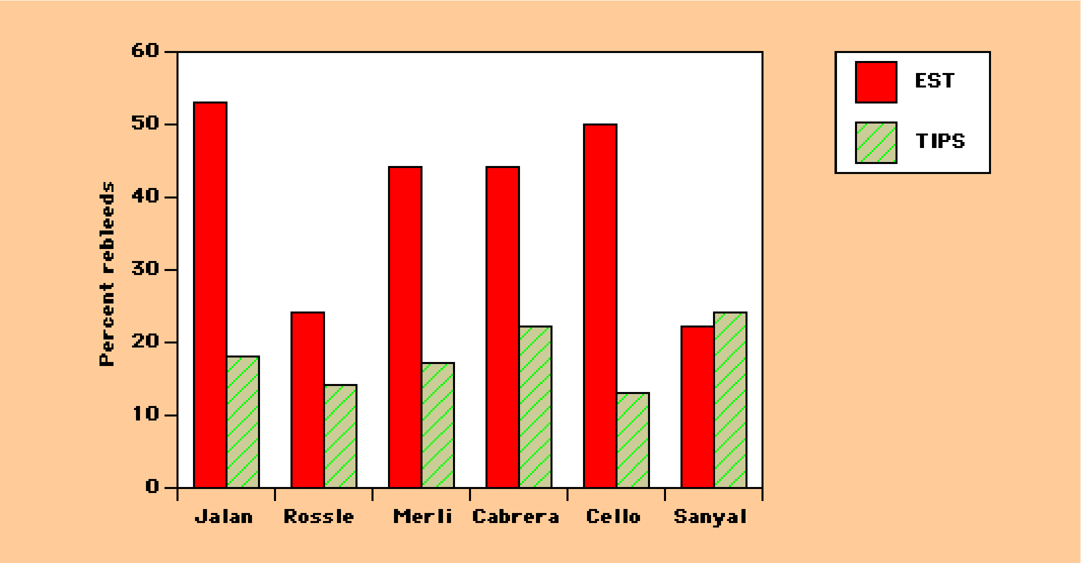
Endoscopic Variceal *Ligation*

- ☐ **Placement of elastic O ring ligatures on varices, causing strangulation of veins**
- ☐ **Original EVL one band & endoscope removed to reload a new band after each ligation.**
- ☐ **Overtube used to facilitate repeated intubation**
- ☐ **Multiple-band devices have now replaced the original single-band device, thereby allowing the deployment of 6 to 10 rubber bands with a single oesophageal intubation**

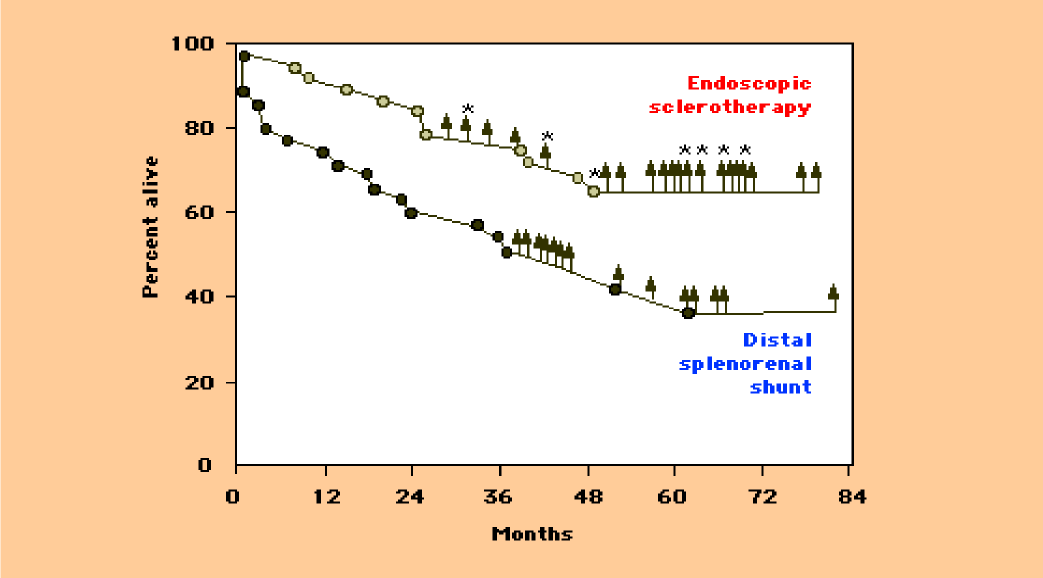
Complications of Variceal *Banding*

- ☐ **EVL = same sedation required for EST**
- ☐ **All Complications less in EVL than EST**
  - ■ **Strictures**
  - ■ **Bleeding from treatment-induced ulcers**
  - ■ **Pulmonary infection**
  - ■ **Bacterial peritonitis**

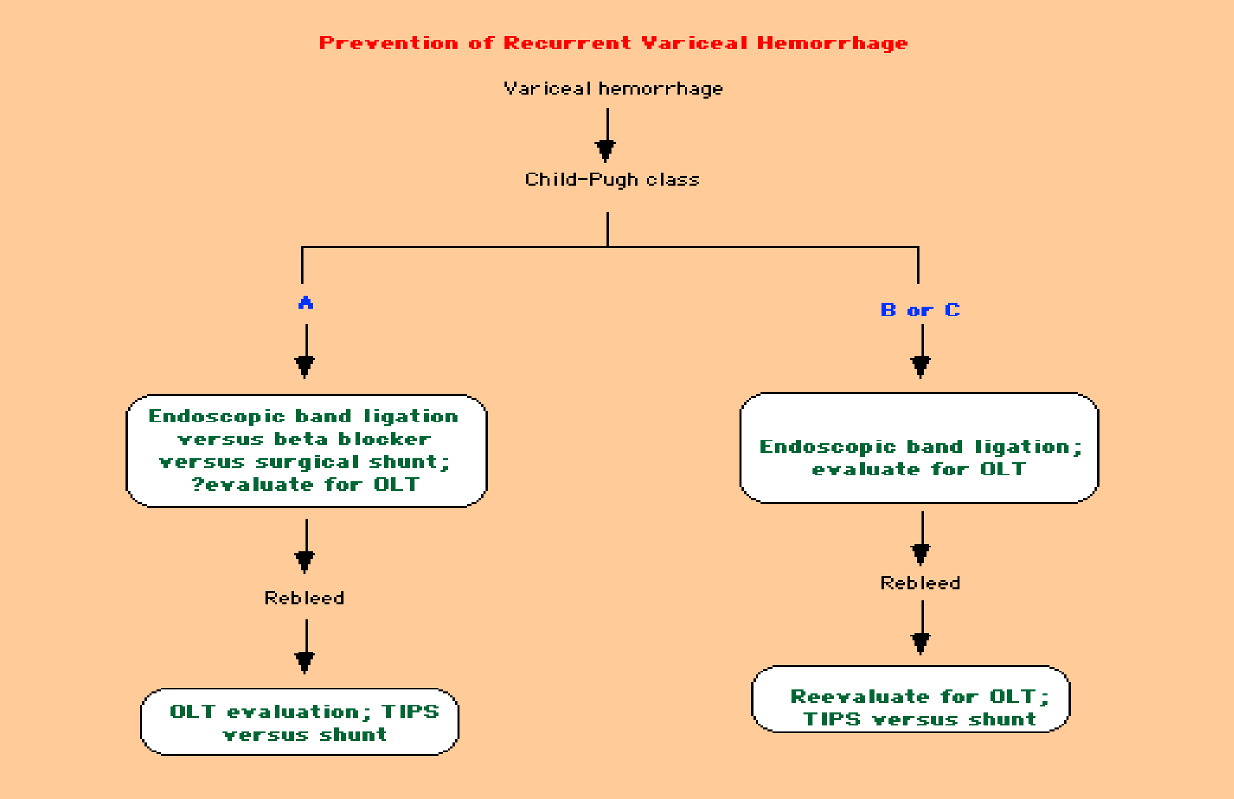
    - **Death**
- ☐ **Multiple-band ligatures prevented compl.of *overtube***
- **EVL Vs EST**
- ☐ **Less complications**
- ☐ **More effective**
- ☐ **Better in preventing rebleeding**
- ☐ **Less number of sessions till eradication.**
- ☐ **Not suitable for active bleeding**
- ☐ **More Recurrence**



Lower rebleeding rate with TIPS versus EST Effects of endoscopic sclerotherapy (EST) and transvenous intrahepatic stent shunt (TIPS) on variceal rebleeding rates in published clinical trials of secondary prevention of variceal hemorrhage. All but the last trial showed a significantly lower rate of rebleeding with TIPS. (Data from Jalan, R, et al, Hepatology 1997; 26:1115; Rossle, M, et al, Lancet 1997; 349:1043; Merli, M, et al, Hepatology 1998; 27:48; Cello, JP, et al, Ann Intern Med 1997; 126:858; Cabrera, J, et al, Gastroenterology 1996; 110:832; and Sanyal, AJ, et al, Ann Intern Med 1997; 126:849.)



Worse survival after distal splenorenal shunt Kaplan-Meier survival curves for 72 patients randomized to endoscopic sclerotherapy or a distal splenorenal shunt to prevent recurrent variceal bleeding. Survival was significantly higher with endoscopic sclerotherapy at a median 61-month follow-up. The survival benefit in the sclerotherapy group was due to surgical rescue (indicated by the asterisks) of the 35 percent of patients who failed sclerotherapy. The arrows represent the patients who were still alive (arrows). (Data from Henderson, JM, Surg Clin North Am 1990; 70:405.)

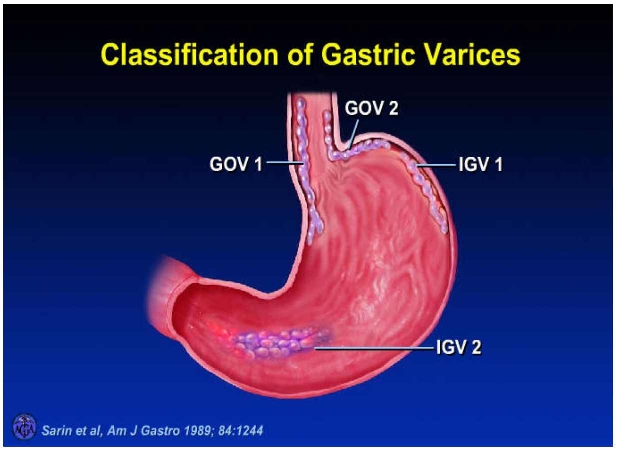


Prevention of Recurrent Variceal Hemorrhage

Variceal hemorrhage
Child-Pugh class
A
B or C
Endoscopic band ligation versus beta blocker versus surgical shunt; ?evaluate for OLT
Endoscopic band ligation; evaluate for OLT
Rebleed
Rebleed
OLT evaluation; TIPS versus shunt
Reevaluate for OLT; TIPS versus shunt

Gastric varices

Classification of Gastric Varices


Classification of Gastric Varices

Sarin et al, Am J Gastro 1989; 84:1244

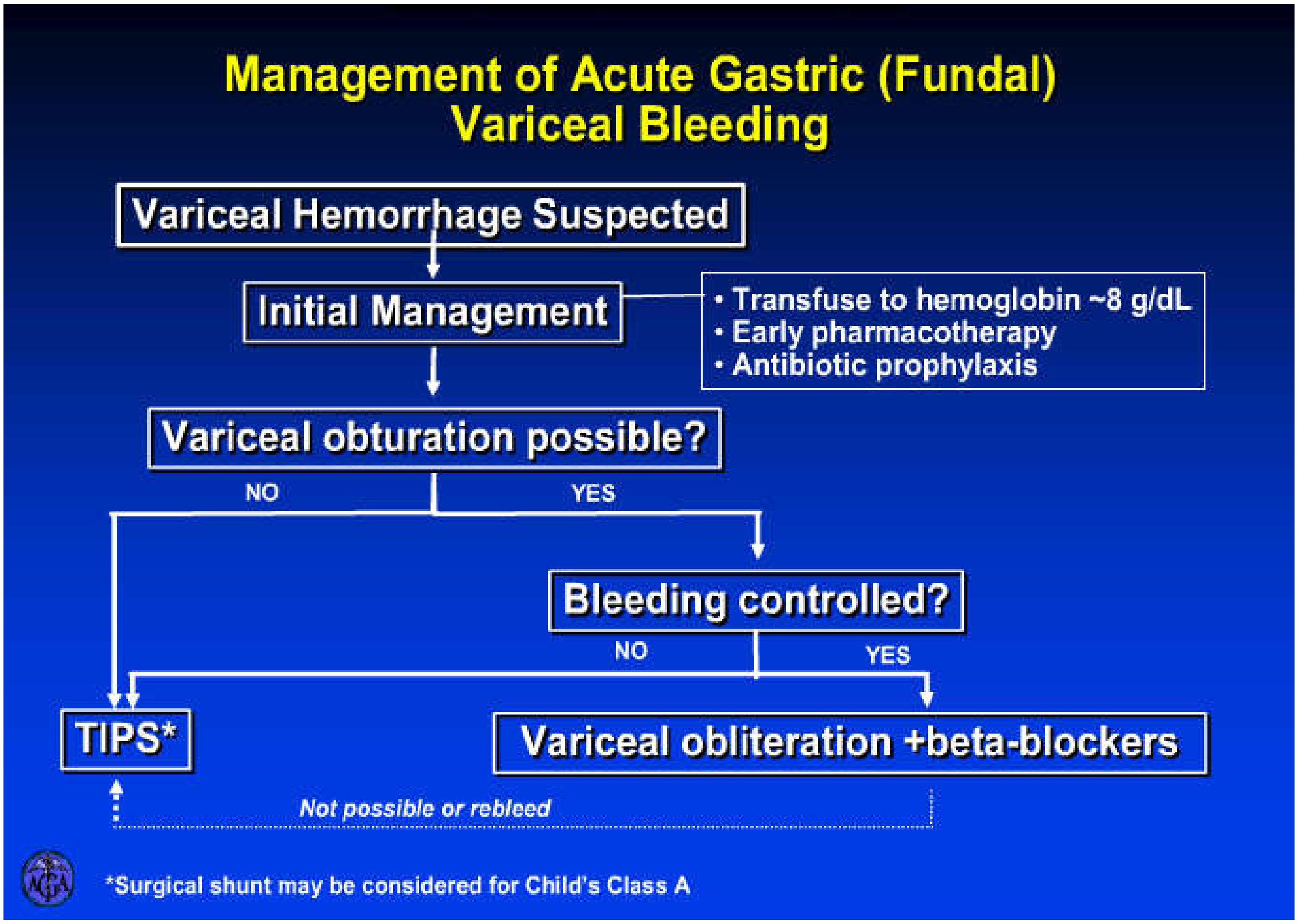
- ☐ Gastro esophageal Varices — GOV
  - ■ Lesser curve - — GOV 1
  - ■ Greater curve - — GOV 2
- ☐ Isolated Gastric Varices — IGV
  - ■ Fundal — IGV – 1
    - ☐ Type I — Junctional
    - ☐ Type II — Fundal
    - ☐ Type III — Linear
  - ■ Antral or body — IGV - 2
- ○ Rare varices
- ☐ Antral
- ☐ Duodenal
- ☐ Rectal

Treatment of Gastric Varices
What is peculiar

- Pharmacologic Rx can stop active bleeding.
- EST : ulceration without variceal obliteration.
- B-blockers may reduce risk of recurrent hge.

Gastric Varices
What is peculiar ?

- Isolated gastric varices may occur in splenic vein thrombosis resulting from pancreatitis, trauma, or other causes.
- Splenectomy is treatment of choice in this setting and is typically curative.



Management of Acute Gastric (Fundal) Variceal Bleeding

Variceal Hemorrhage Suspected

Initial Management

- Transfuse to hemoglobin ~8 g/dL
- Early pharmacotherapy
- Antibiotic prophylaxis

Variceal obturation possible?

NO

YES

Bleeding controlled?

NO

YES

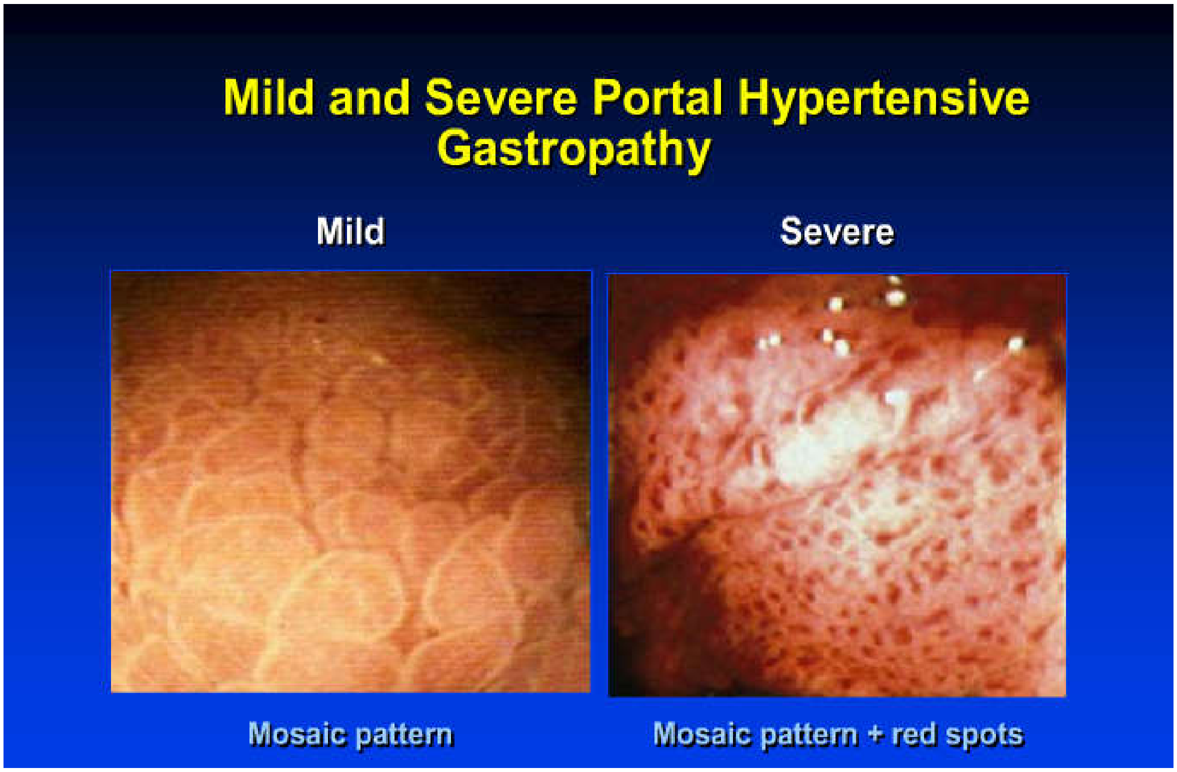
TIPS*

Variceal obliteration +beta-blockers

Not possible or rebleed

*Surgical shunt may be considered for Child's Class A

Portal Hypertensive Gastropathy



Mild and Severe Portal Hypertensive Gastropathy

Mild

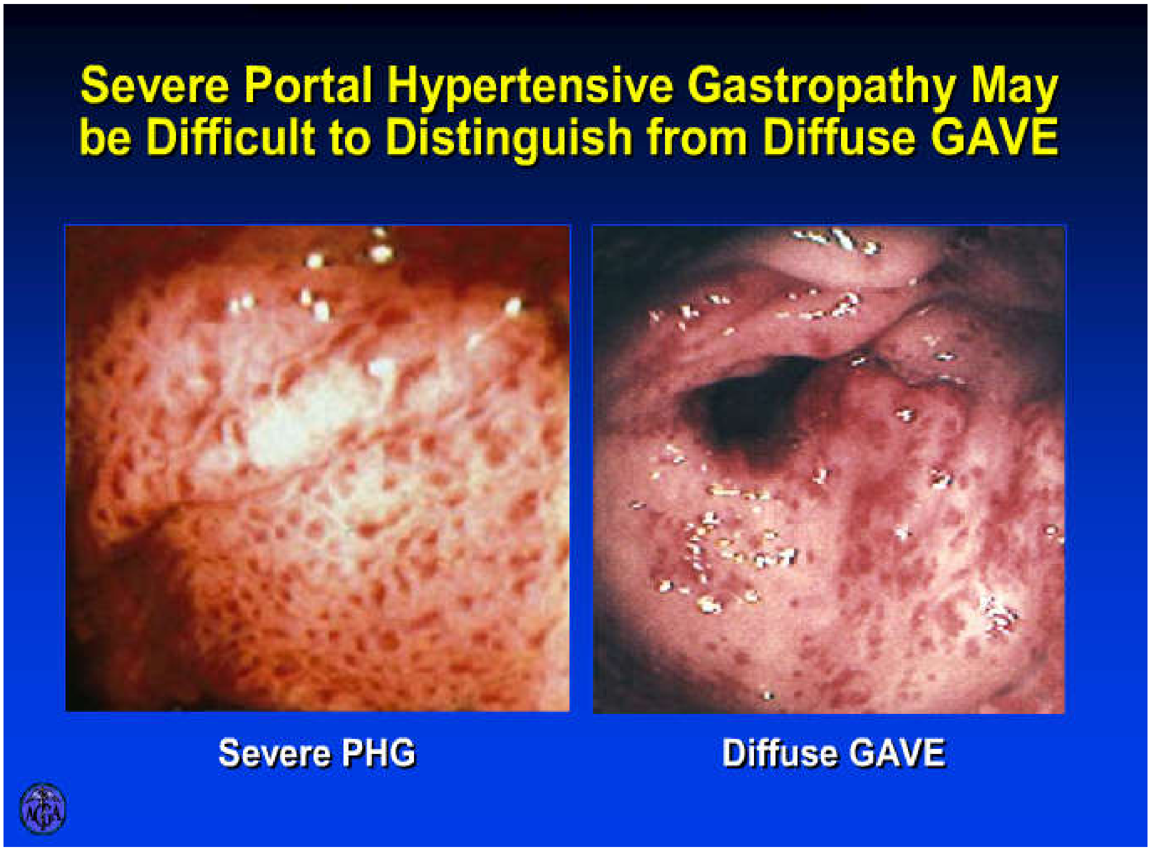
Severe

Mosaic pattern

Mosaic pattern + red spots

Classification of Portal Hypertensive Gastropathy

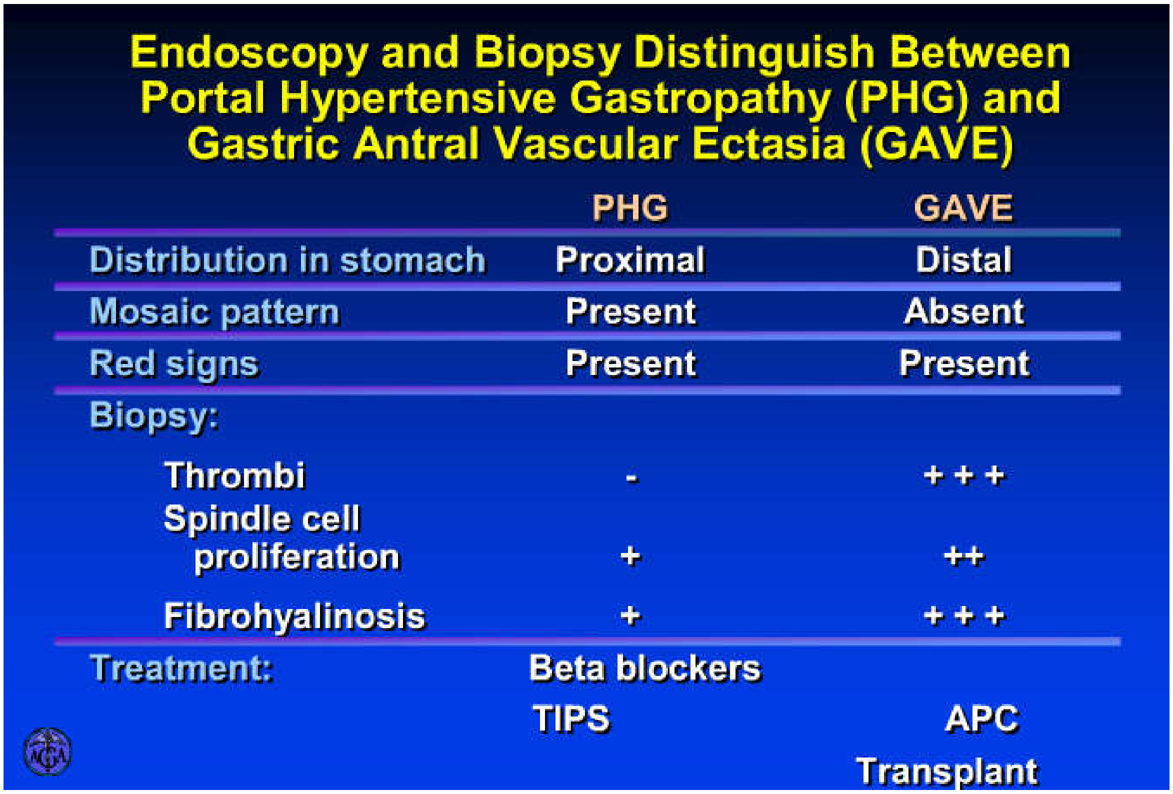
	Mild	Severe
Endoscopic features	Mosaic pattern	Mosaic pattern Red spots
GI Blood loss	No	Yes
Treatment	No	Beta blockers TIPS



Severe Portal Hypertensive Gastropathy May be Difficult to Distinguish from Diffuse GAVE

Severe PHG

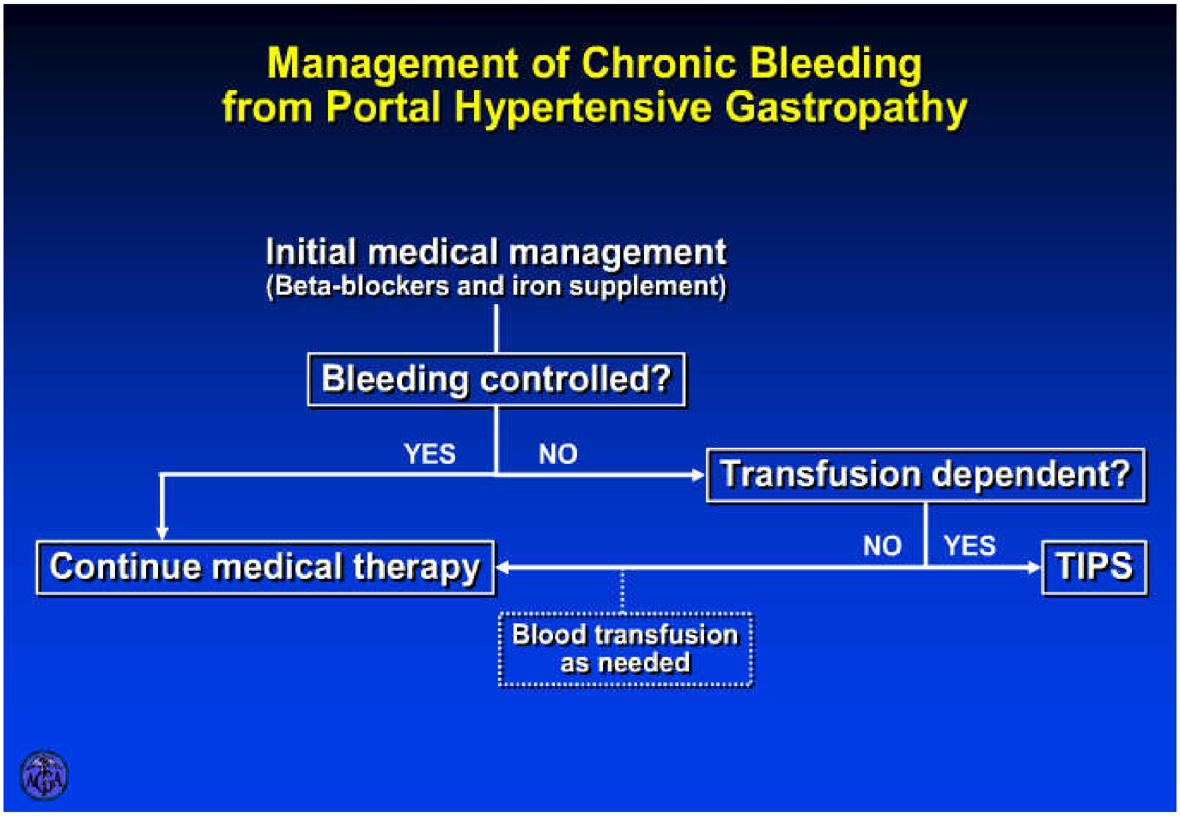
Diffuse GAVE



Endoscopy and Biopsy Distinguish Between Portal Hypertensive Gastropathy (PHG) and Gastric Antral Vascular Ectasia (GAVE)

	PHG	GAVE
Distribution in stomach	Proximal	Distal
Mosaic pattern	Present	Absent
Red signs	Present	Present
Biopsy:		
Thrombi	-	+ + +
Spindle cell proliferation	+	++
Fibrohyalinosis	+	+ + +
Treatment:	Beta blockers TIPS	APC Transplant

- Bleeding from PHG
    - Occult
    - Acute hemorrhage (rare)
- % of pts bleeding from PHG at 1 year :
    - 35% on propranolol
    - 62% on placebo.



Management of Chronic Bleeding from Portal Hypertensive Gastropathy

Initial medical management
(Beta-blockers and iron supplement)

Bleeding controlled?

YES

NO

Transfusion dependent?

Continue medical therapy

NO

YES

TIPS

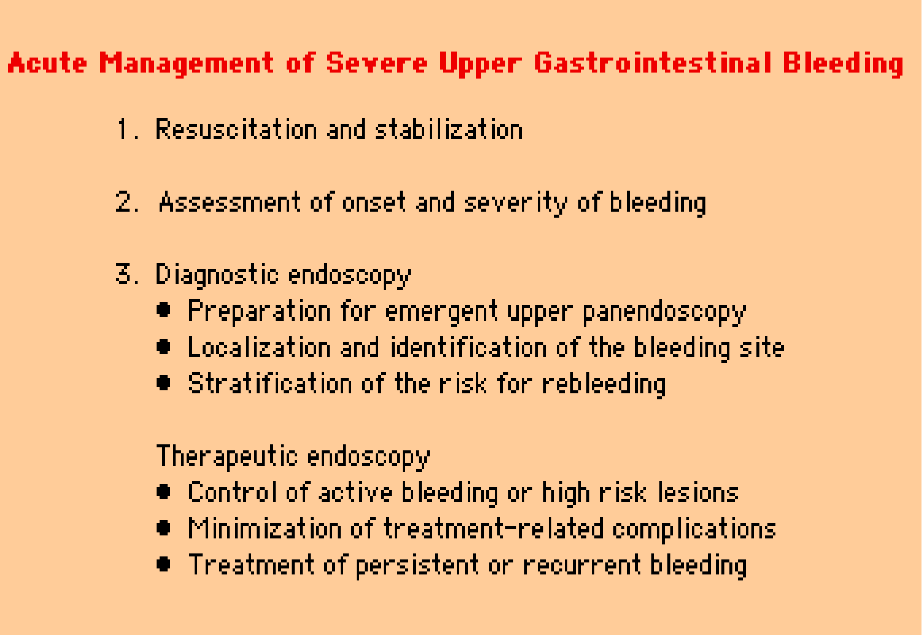
Blood transfusion as needed

Treatment of PHG

- APC - Argon Plasma Coagulation
- Portal decompression
    - Portacaval shunt surgery
    - TIPS

Non- Variceal Upper GI Bleeding

- ☐ **PUD**
- ☐ **GERD**
- ☐ **Tumors**
- ☐ **Mallorey Weiss tear**
- ☐ **AV malformation**
- ☐ **Dieulafoy’s Lesion**



Acute Management of Severe Upper Gastrointestinal Bleeding

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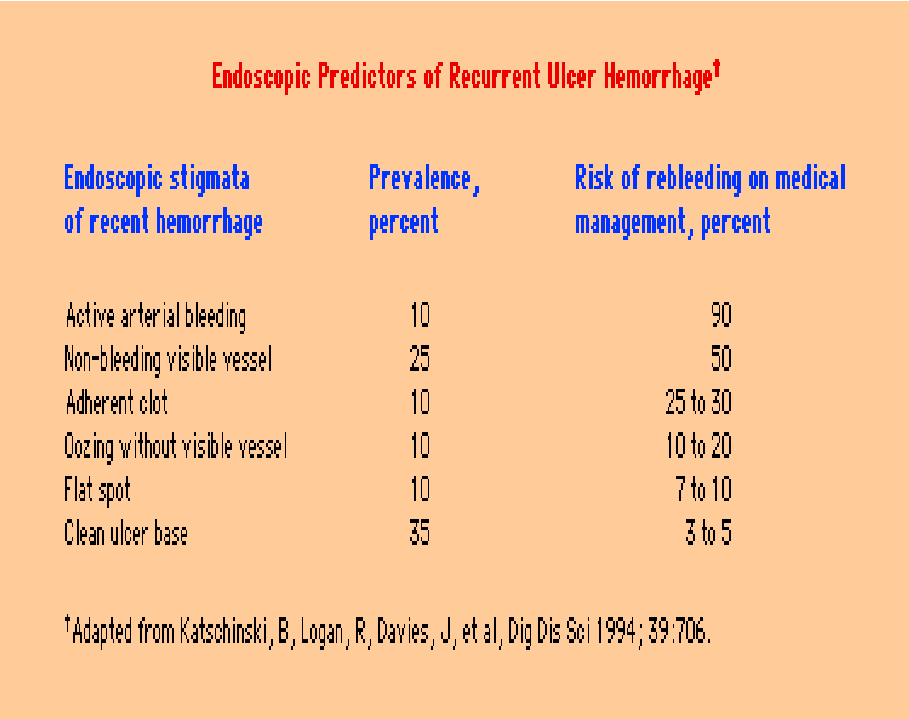
   - Stratification of the risk for rebleeding

   Therapeutic endoscopy
   - Control of active bleeding or high risk lesions
   - Minimization of treatment-related complications
   - Treatment of persistent or recurrent bleeding



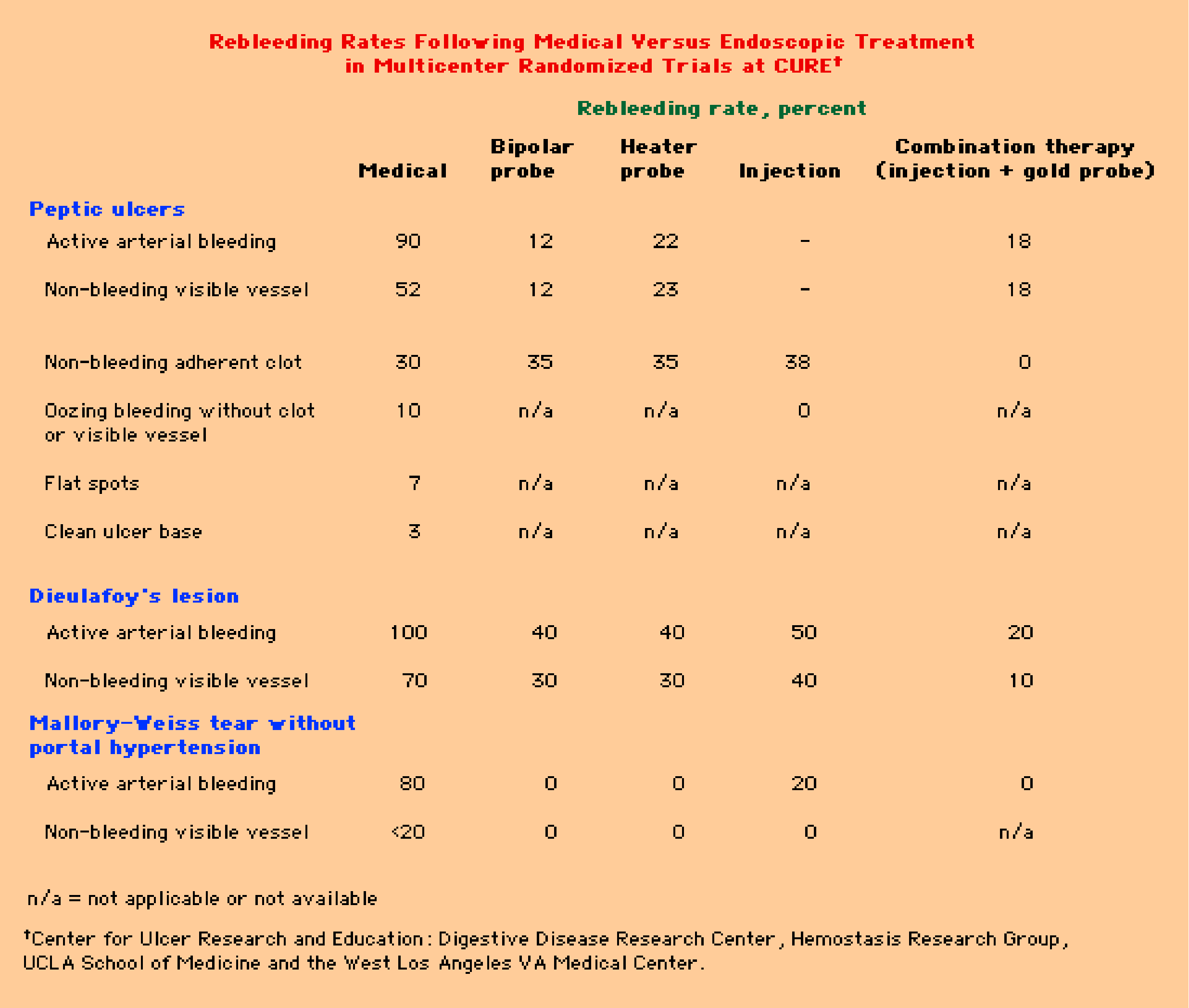
Endoscopic Predictors of Recurrent Ulcer Hemorrhage†

Endoscopic stigmata of recent hemorrhage	Prevalence, percent	Risk of rebleeding on medical management, percent
Active arterial bleeding	10	90
Non-bleeding visible vessel	25	50
Adherent clot	10	25 to 30
Oozing without visible vessel	10	10 to 20
Flat spot	10	7 to 10
Clean ulcer base	35	3 to 5

†Adapted from Katschinski, B, Logan, R, Davies, J, et al, Dig Dis Sci 1994; 39:706.

Treatment of Bleeding Ulcer

- **Endoscopic Methods**
  - **Heater Probe**
  - **Coagulation (monopolar or Bipolar)**
  - **Sclerotherapy**
  - **Band Ligation**
  - **APC**
  - **Laser Therapy**

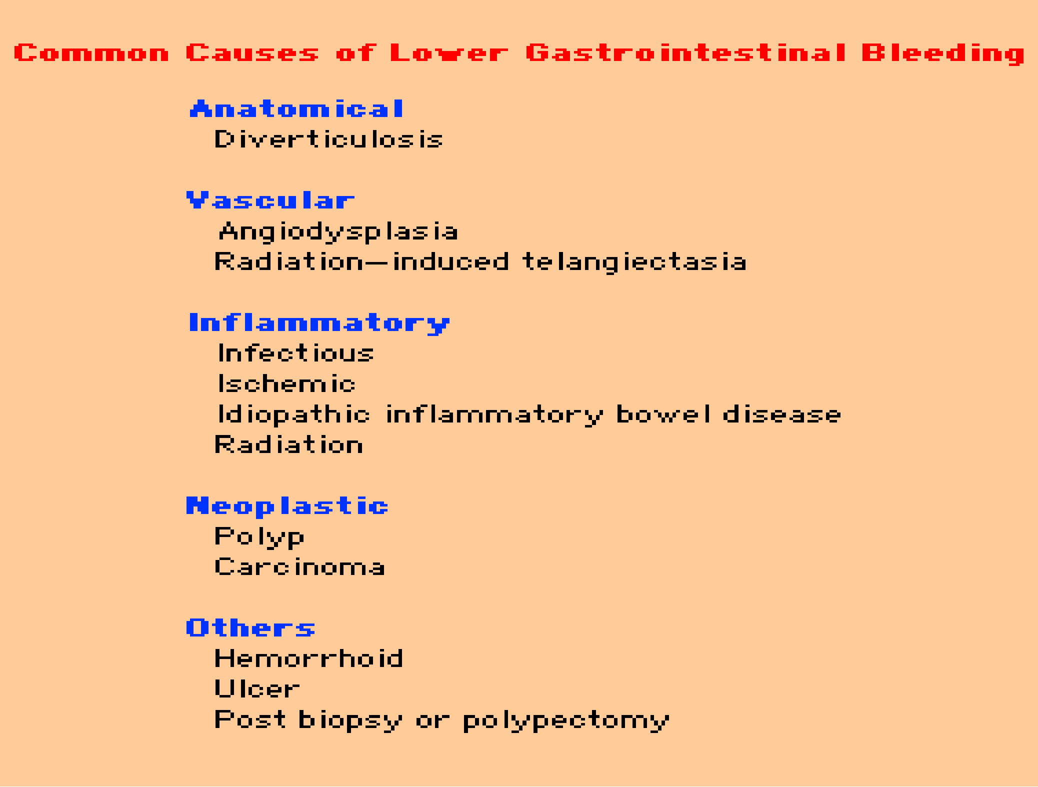


Rebleeding Rates Following Medical Versus Endoscopic Treatment in Multicenter Randomized Trials at CURE[†]

	Rebleeding rate, percent				
	Medical	Bipolar probe	Heater probe	Injection	Combination therapy (injection + gold probe)
Peptic ulcers					
Active arterial bleeding	90	12	22	-	18
Non-bleeding visible vessel	52	12	23	-	18
Non-bleeding adherent clot	30	35	35	38	0
Oozing bleeding without clot or visible vessel	10	n/a	n/a	0	n/a
Flat spots	7	n/a	n/a	n/a	n/a
Clean ulcer base	3	n/a	n/a	n/a	n/a
Dieulafoy's lesion					
Active arterial bleeding	100	40	40	50	20
Non-bleeding visible vessel	70	30	30	40	10
Mallory-Weiss tear without portal hypertension					
Active arterial bleeding	80	0	0	20	0
Non-bleeding visible vessel	<20	0	0	0	n/a

n/a = not applicable or not available

[†] Center for Ulcer Research and Education: Digestive Disease Research Center, Hemostasis Research Group, UCLA School of Medicine and the West Los Angeles VA Medical Center.



Common Causes of Lower Gastrointestinal Bleeding

Anatomical
- Diverticulosis

Vascular
- Angiodysplasia
- Radiation—induced telangiectasia

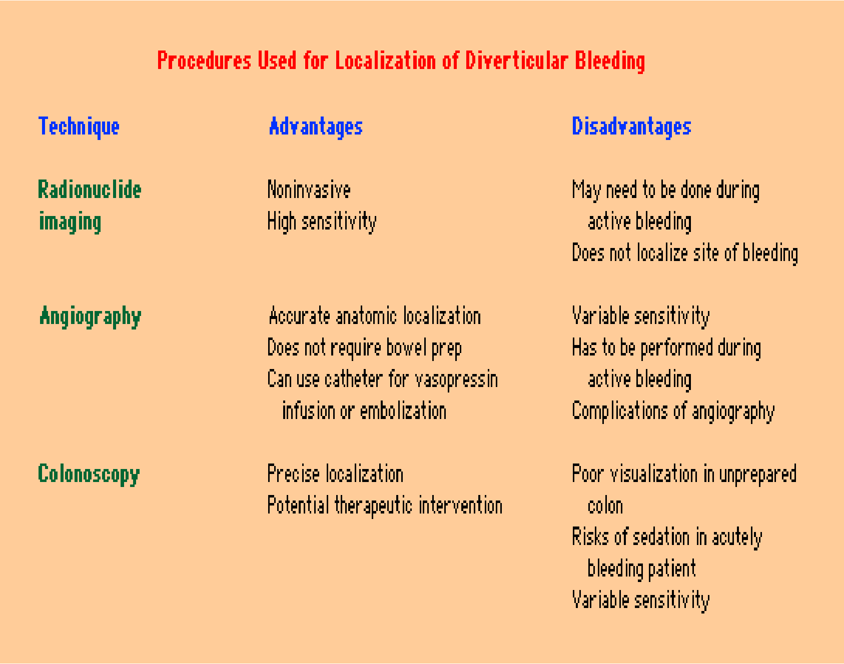
Inflammatory
- Infectious
- Ischemic
- Idiopathic inflammatory bowel disease
- Radiation

Neoplastic
- Polyp
- Carcinoma

Others
- Hemorrhoid
- Ulcer
- Post biopsy or polypectomy

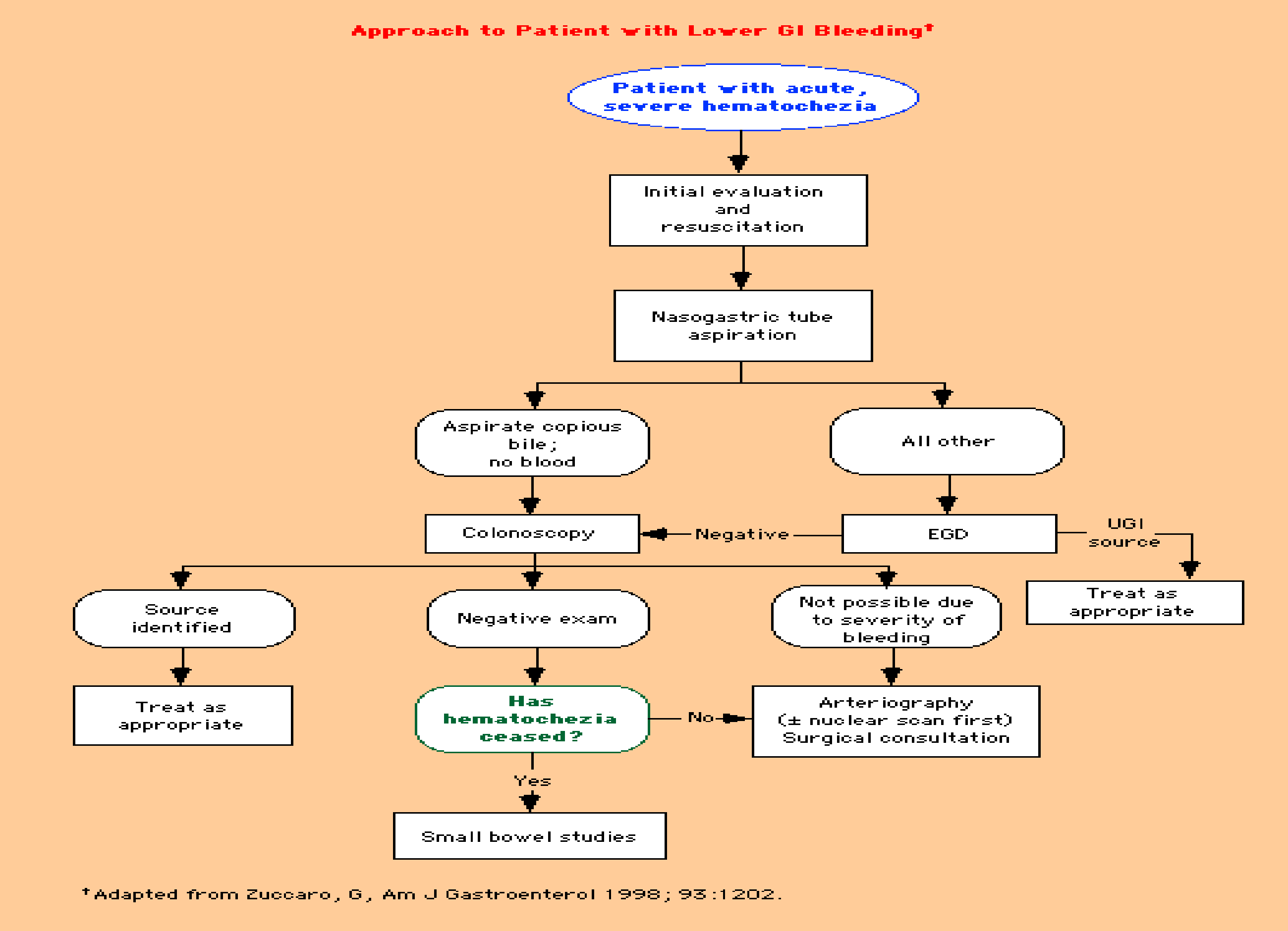
Methods of Diagnosis :

Colonoscopy Radionucleide Scanning Angiography



Procedures Used for Localization of Diverticular Bleeding

Technique	Advantages	Disadvantages
Radionuclide imaging	Noninvasive High sensitivity	May need to be done during active bleeding Does not localize site of bleeding
Angiography	Accurate anatomic localization Does not require bowel prep Can use catheter for vasopressin infusion or embolization	Variable sensitivity Has to be performed during active bleeding Complications of angiography
Colonoscopy	Precise localization Potential therapeutic intervention	Poor visualization in unprepared colon Risks of sedation in acutely bleeding patient Variable sensitivity



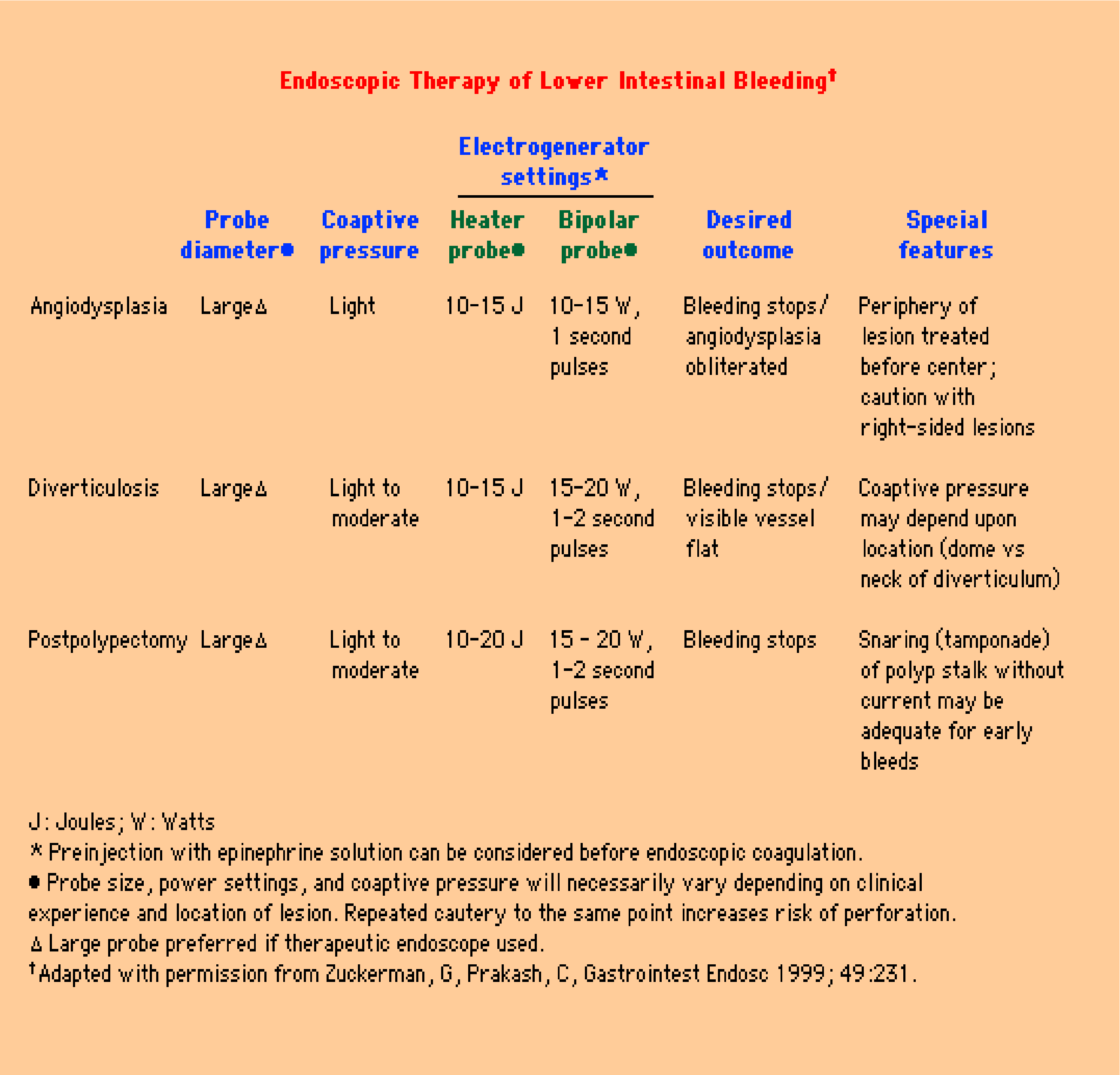
Approach to Patient with Lower GI Bleeding*

Patient with acute, severe hematochezia
Initial evaluation and resuscitation
Nasogastric tube aspiration
Aspirate copious bile; no blood
All other
Colonoscopy
Negative
EGD
UGI source
Treat as appropriate
Source identified
Negative exam
Not possible due to severity of bleeding
Treat as appropriate
Has hematochezia ceased?
No
Arteriography (± nuclear scan first) Surgical consultation
Yes
Small bowel studies

*Adapted from Zuccaro, G, Am J Gastroenterol 1998; 93:1202.

Endoscopic Methods of Rx

- ☐ Heater Probe
- ☐ Coagulation
- ☐ Laser
- ☐ APC
- ☐ Band Ligation
- ☐ Loops
- ☐ Clips



Endoscopic Therapy of Lower Intestinal Bleeding[†]

			Electrogenerator settings*			
	Probe diameter●	Coaptive pressure	Heater probe●	Bipolar probe●	Desired outcome	Special features
Angiodysplasia	Large∆	Light	10-15 J	10-15 W, 1 second pulses	Bleeding stops/ angiodysplasia obliterated	Periphery of lesion treated before center; caution with right-sided lesions
Diverticulosis	Large∆	Light to moderate	10-15 J	15-20 W, 1-2 second pulses	Bleeding stops/ visible vessel flat	Coaptive pressure may depend upon location (dome vs neck of diverticulum)
Postpolypectomy	Large∆	Light to moderate	10-20 J	15 - 20 W, 1-2 second pulses	Bleeding stops	Snaring (tamponade) of polyp stalk without current may be adequate for early bleeds

J: Joules; W: Watts

* Preinjection with epinephrine solution can be considered before endoscopic coagulation.

● Probe size, power settings, and coaptive pressure will necessarily vary depending on clinical experience and location of lesion. Repeated cautery to the same point increases risk of perforation.

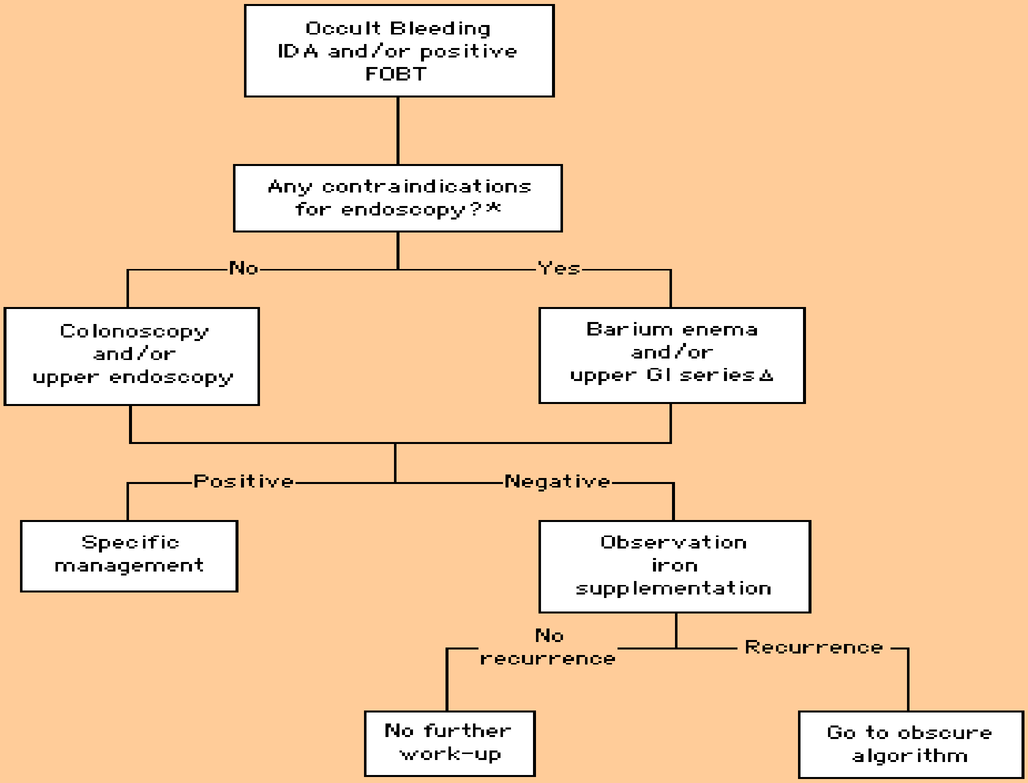
∆ Large probe preferred if therapeutic endoscope used.

[†] Adapted with permission from Zuckerman, G, Prakash, C, Gastrointest Endosc 1999; 49:231.

Occult GI Bleeding

- ☐ Occult positive Stools (FOBT)
- ☐ Iron Deficiency Anemia (IDA)

Evaluation of Occult Bleeding†

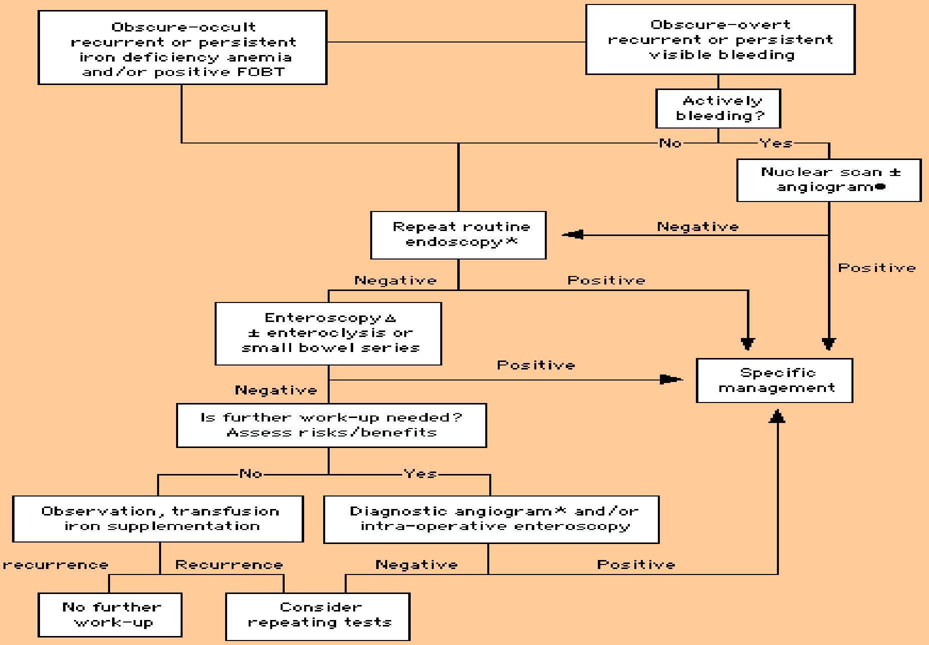

Occult Bleeding IDA and/or positive FOBT
Any contraindications for endoscopy?*
No
Yes
Colonoscopy and/or upper endoscopy
Barium enema and/or upper GI series∆
Positive
Negative
Specific management
Observation iron supplementation
No recurrence
Recurrence
No further work-up
Go to obscure algorithm

Algorithm for evaluation of occult bleeding. *The indication and sequence of endoscopic procedures may be directed by patient age, symptoms, and comorbid conditions; small bowel biopsy is indicated at this juncture only in the presence of clinical or endoscopic evidence of celiac sprue. ∆Radiological studies may be indicated when comorbid conditions make endoscopy risky or when endoscopy is incomplete; small bowel follow-through radiographs have a very low yield unless clinical evidence exists for small bowel disease.
†Reproduced with permission from the American Gastroenterological Association. Zuckerman, GR, Prakash, C, Askin, MP, Lewis, BS, Gastroenterology 2000; 118:201.

Obscure GI Bleeding

- ☐ Obscure Occult
  - FOBT
  - IDA
- ☐ Obscure Overt
  - Rec. Visible Bleeding

Evaluation of Obscure Bleeding†


Obscure-occult recurrent or persistent iron deficiency anemia and/or positive FOBT
Obscure-overt recurrent or persistent visible bleeding
Actively bleeding?
No
Yes
Nuclear scan ± angiogram●
Repeat routine endoscopy*
Negative
Positive
Negative
Positive
Enteroscopy∆ ± enteroclysis or small bowel series
Positive
Specific management
Negative
Is further work-up needed? Assess risks/benefits
No
Yes
Observation, transfusion iron supplementation
Diagnostic angiogram* and/or intra-operative enteroscopy
No recurrence
Recurrence
Negative
Positive
No further work-up
Consider repeating tests

*The decision to repeat upper endoscopy and/or colonoscopy may depend on the skill and expertise of the initial endoscopist; push enteroscopy can replace upper endoscopy at this juncture; and small bowel biopsy is indicated in patients with clinical or endoscopic evidence of celiac sprue or unexplained iron deficiency anemia (IDA).

●Repeat routine endoscopy may be performed in actively bleeding patients at the discretion of the endoscopist.

∆Push enteroscopy and/or Sonde enteroscopy may be performed, depending on operator and institution expertise; enteroclysis can complement enteroscopy and improve the diagnostic yield. Angiography performed electively may demonstrate typical findings of angiodysplasia or a tumor blush.

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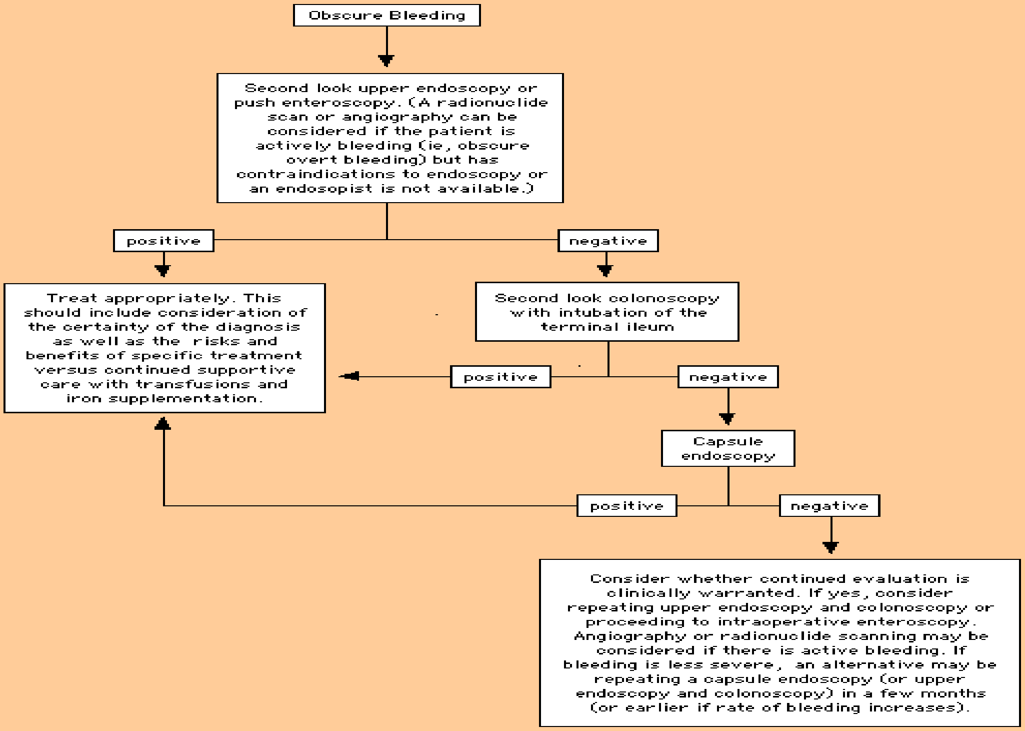
Obscure Bleeding
Second look upper endoscopy or push enteroscopy. (A radionuclide scan or angiography can be considered if the patient is actively bleeding (ie, obscure overt bleeding) but has contraindications to endosocopy or an endosopist is not available.)
positive
negative
Treat appropriately. This should include consideration of the certainty of the diagnosis as well as the risks and benefits of specific treatment versus continued supportive care with transfusions and iron supplementation.
Second look colonoscopy with intubation of the terminal ileum
positive
negative
Capsule endoscopy
positive
negative
Consider whether continued evaluation is clinically warranted. If yes, consider repeating upper endoscopy and colonoscopy or proceeding to intraoperative enteroscopy. Angiography or radionuclide scanning may be considered if there is active bleeding. If bleeding is less severe, an alternative may be repeating a capsule endoscopy (or upper endoscopy and colonoscopy) in a few months (or earlier if rate of bleeding increases).